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No. 4, 1977

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PRINCIPAL METHODS OF SIMULATING BIOLOGICAL EFFECTS OF WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 3-9

[Article by Ye. A. Kovalenko, submitted 11 Apr 1975]

[Text] At the present time, one of the prominent problems of space biology and medicine is to make a comprehensive study of the distinctions of effects on man of prolonged weightlessness. Of course, this requires extensive ground-based research with more or less complete simulation of various aspects of the effects of weightlessness on the organism. This approach to the problem of weightlessness is much more economical than obtaining extremely valuable, but limited and, unfortunately, sporadic data obtained as a result of missions. In addition, with simulation of biological effects of weightlessness on earth, it is possible to conduct studies on virtually all levels of biological organization of living systems using the latest methodological procedures.

In this work, an effort is made to systematize some methods of simulating and modeling the effects of weightlessness on the living organism under ground-based conditions.

The methods of partial simulation of the effects of weightlessness under ground-based conditions are based on the feasibility of reproducing some elements [1-3] of the mechanism of the effects of weightlessness on the organism. We can distinguish three main categories of modeling: 1) decreasing the effect of gravity on the organism; 2) creating a variable effect of gravity on the organism and 3) simulation of different effects of pathogenesis of weightlessness on the organism by means of biological procedures (see Figure 1).

Each of these categories can, in turn, be divided into groups of specific methods of modeling weightlessness.

First Category: Reduction of Effects of Gravity on the Organism

A. Prolonged Submersion in Fluid

Under ordinary conditions, when earth's gravitation affects all parts of the body, the organism is, so to speak, "loaded" with gravitation forces all over the body mass. At the same time, the force of the support reaction acts on the feet. As a result of these opposite forces, the entire organism and all parts of the body experience tension [pressure] and strain [deformation] perceived by them as the effect of weight force. Tension strains increase with man in a vertical position, in the direction from the top to the bottom parts of the body, reaching a maximum in the legs, and particularly their lower parts, the feet (Figure 2a).

When man submerges in a fluid (Figure 3a) with a specific gravity close to mean specific gravity of the body, there is virtually identical distribution of the effect of the body's force of gravity on the surface of the liquid in contact with the body. Moreover, in accordance with the law of Archimedes, the body is affected by a buoyant force which equals the weight of the displaced fluid. It is expressly through such change in nature of effects of forces on the body that it is possible to simulate some of the physiological effects of weightlessness. At the same time, the internal organs and internal parts of the body continue to be exposed to the force of earth's gravity, as they were before submerging. The otolith system also continues to inform the organism about the direction of the vector of earth's gravitation. True, under these conditions, strain and tension not only of external, but partially of internal parts of the body could be diminished to some extent, due to the larger support surfaces and fluid pressure. It is also important that, with submersion in vertical position (see Figure 3b), there is compensation for hydrostatic blood pressure in vessels by the corresponding counterpressure of surrounding fluid on the surface of the body and tissues surrounding the vessels. Compensation and elimination of the hydrostatic factor are one of the most important advantages of the method, which permits investigation of the effects of weightlessness on the cardiovascular system. Its flaws are as follows: rapid movement is difficult in liquid media; respiration is somewhat difficult due to compression of the chest by the liquid; it is not always possible to maintain a comfort-level temperature; there are additional psychological and sensory stimuli. The prolonged exposure of the skin to a liquid medium could elicit maceration; for this reason, special fluids (for example, silicon) are occasionally used, or else some special types of light-weight, waterproof clothing. In recent years, the method of "dry" submersion began to be used, involving special, waterproof, but very elastic fabric. In this case, the skin does not come in direct contact with the fluid [4-6].

B. Prolonged Bed Rest and Hypokinesia

Prolonged bed rest (see Figure 3c) simulates well primarily partial elimination of the effects of force of gravity of upper parts of the body on lower

parts, with appreciable decrease in body strain, muscle tension and load on the bones. Gravity is distributed over wide support areas (see Figure 2b). It is also important that this is associated with shifting of fluids of the organism and elimination of hydrostatic pressure. The redistribution of fluids and blood induces a chain of changes in the circulatory system, as well as related disturbances referable to fluid and electrolyte metabolism. With bed rest, there is also a significant decrease in range of general muscular activity, since an individual lying in bed does not perform the usual amount of operations inherent in an active mode of life. All this reduces oxygen intake and load on the cardiovascular system. As a result there is summation of effects induced by horizontal body position and hypokinesia proper. There is an appreciable decrease in intensity of function of the muscles and virtually all systems of the organism [7-10].

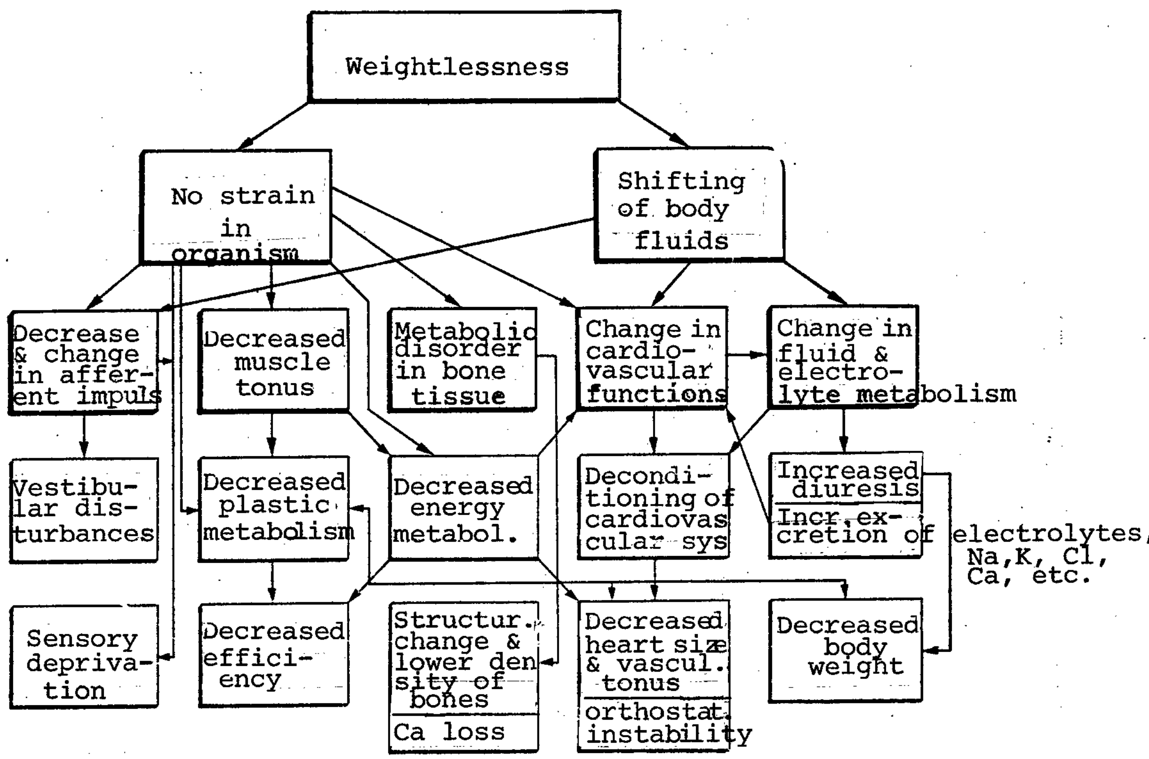
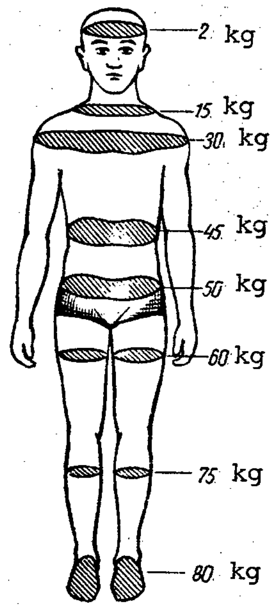
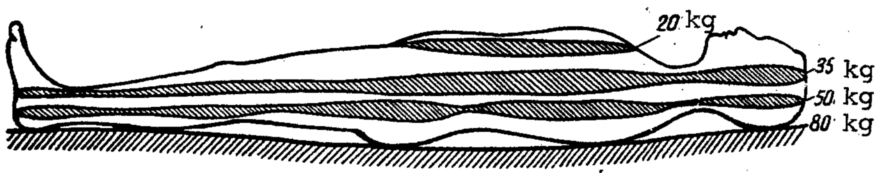


Figure 1. Overall diagram of mechanism of effects of prolonged weightlessness on the organism

In recent years, some new variants of this method have also been used. In the course of prolonged bed rest, the subjects are not in a strictly horizontal position; rather, the head of the bed is slightly tilted down (antiorthostasis), which intensifies redistribution of blood and body fluids to the upper half of the body. Thus, one of the most important elements of the mechanism of effects of weightlessness on the organism are simulated to a large extent, leading to subsequent changes in hemodynamics, fluid and electrolyte metabolism and redistribution of fluids in the organism [8, 11].

Figure 2.
Approximate distribution of pressure of upper parts of body on lower ones with the body in vertical (a) and horizontal (b) position





Prolonged hypokinesia in seated position (see Figure 3d) is used less often as a method of simulating weightlessness. In this case there is approximate simulation of reduced muscular exertion (far from the full range), as compared to that involved on earth to overcome the force of gravity [3, 7-9, 12].

Bed rest and hypokinesia as such have some advantages over other ground-based methods of modeling, because of their simplicity.

To date, many valuable data have been obtained to confirm the great similarity of changes occurring in some functions after weightlessness and prolonged hypokinesia [1-3, 7-19].

C. Use of Stands to Simulate Weightlessness

The use of special stands, with diminished support reactions, in which a man or animal is suspended on straps (a small balloon can also be used) is a unique method of partial simulation of the effects of weightlessness [20-23]. Here, the load on the skeletomuscular system is markedly reduced (see Figure 3, e, g, f). The suspension points are usually situated either close

to the body's center of gravity, or the centers of gravity of different parts of the body. These procedures can obtain an appreciable decrease in load on the muscular system and skeleton, as well as expenditure of energy. If one uses a stand with a steeply inclined support plane (see Figure 3g) the effect of forces of gravity becomes almost perpendicular to the longitudinal axis of the body, and there is partial removal of hydrostatic blood pressure. Simulation of the biological effects of weightlessness with the use of devices with decreased support reaction is generally used for the study of efficiency, coordination of movements and expenditure of energy under conditions of sharp reduction of the effect of force of gravity on the organism [23].

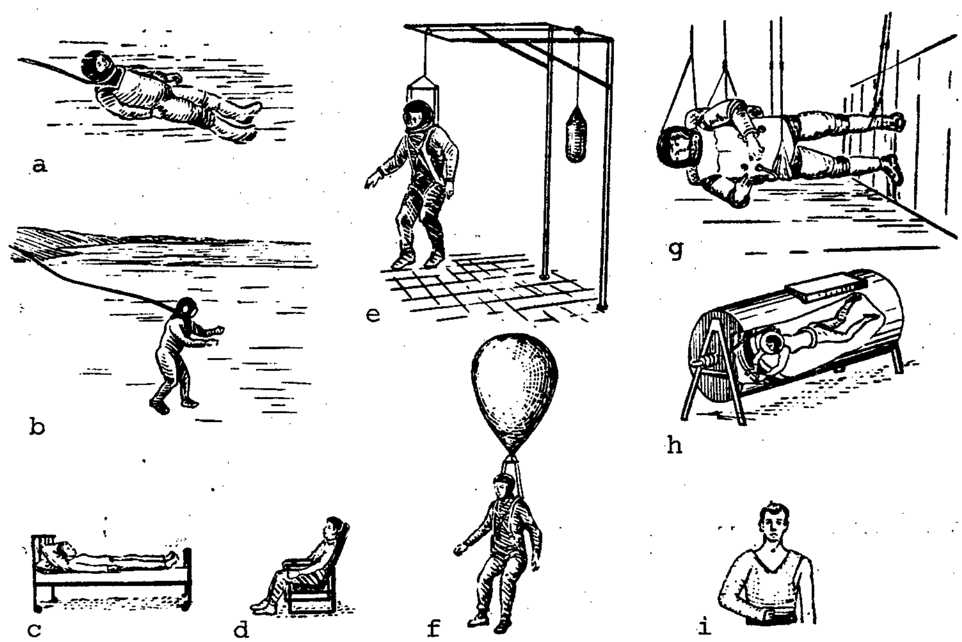


Figure 3. Ground-based modeling of weightlessness

a and b) submersion in water, in horizontal and vertical position
c and d) hypokinesia in supine and seated position
e, f, g) various means of lowering support reaction
h) submersion in water contained in a revolving device

Second Category: Creating Variable Effect of Gravity on the Organism

A. Brief Rotation on a Centrifuge

If an individual is rotated on a centrifuge and exposed to up to 1 G in the pelvis-head direction, one can obtain, in a hyperbolized form, the effect of redistribution of blood from the lower half of the body to the upper and, in addition, several subjective sensations inherent in weightlessness. In

some cases, it is very convenient to obtain expressly such a hyperbolized effect, since it helps demonstrate more distinction, to observe and, consequently, to investigate the mechanisms of changes that occur, primarily in the cardiovascular system, in weightlessness.

B. Prolonged Rotation on a Centrifuge

The next form of simulation of weightlessness is prolonged rotation on a centrifuge with a small G force in the head-pelvis direction. It is assumed that the effects observed in weightlessness will be opposite to these. Evidently, this principle is quite hypothetical. However, under some conditions, this approach and extrapolations may be rather useful. In this case, particularly if we wish to increase tissular strain and shifting of body fluids, i.e., two of the main elements lacking in weightlessness, we shall obtain data in an opposite and markedly intensified form.

If a low G force is created in the head-pelvis direction for a long time and the direction is then rapidly reversed, and a head-pelvis load is again created, this situation could simulate, to some extent, the effects that occur with the transition from earth's gravity to weightlessness and back, from weightlessness to earth's gravitation. This unique approach could be used more for simulation and comprehensive investigation of the transient processes at the start and end of a mission.

Finally, it is possible to create changes from large acceleration to small and vice versa, with rather long exposure, on a centrifuge. Of course, here too, there is quite approximate simulation of the changes from earth's gravity to weightlessness and from the prolonged effect of weightlessness to earth's gravitation.

Unfortunately, in such cases, it is difficult to create strictly quantitative correspondence of this exposure to the real conditions of weightlessness, and we cannot rule out the specific effects of rotation itself. However, the very principle of increasing or decreasing, as well as changing the direction of inertial forces on the organism merits considerably more attention in experimental practice. If a plant is rotated about an axis that forms a right angle with the vector of gravitation, at a speed that does not elicit any pathological changes, sedimentation or shifting of suspended particles, one can equalize, to some extent, the constant and usually strictly directed effect of earth's gravity [24]. This procedure (see Figure 3h) has been used occasionally to rotate animals and man in a lateral position under special conditions, and even in water [25].

Third Category: Simulation of Different Pathogenetic Effects of Weightlessness on the Organism by Means of Biological Procedures

A. Partial Immobilization

In order to simulate the local effect of weightlessness on different parts of the body, one can use various forms of immobilization, such as plaster casts, bandages and splints (see Figure 3i), and even sever the ligaments

in experiments on animals [26]. However, in such cases, there is greater restriction of limb movements than in weightlessness, and this must be taken into consideration in analyzing the obtained data. Furthermore, this means of simulation may elicit additional functional disturbances that are not inherent in the prolonged effect of weightlessness. This modeling method should be used in the study of regional disturbances of plastic and energy metabolism, as well as to produce severe morphological, histochemical and biochemical changes reflecting the extreme degree of disturbances that are possible after a very long period of weightlessness.

B. Denervation

Animals develop much greater disturbances after total or partial denervation of some part of the body than in weightlessness. However, occasionally this is precisely what is required for more definite determination of the direction of processes. The advantage is that one can separately simulate elimination of the afferent or efferent element of neural regulation and study the functional, particularly trophic, changes occurring in muscles. However, this simulation method does not reflect exactly the potential consequences of weightlessness.

The use of various pharmacological methods of excluding muscular function is an original method of simulation. In such cases, it is possible to obtain rather distinct disturbances, referable to functions, as well as metabolic processes in muscles, against the background of myorelaxation [17].

C. Other Physiological Procedures

One can, for example, redistribute the mass of circulating blood and change the volumes thereof by using pumps in some parts of the blood stream. One can produce certain changes in fluid and electrolyte metabolism, artificially induce the Henry-Gauer reflex by stimulating specific centers or nerves. These phenomena can also be produced by infusing an additional large amount of blood (or blood substitutes), or hormones (antidiuretic hormone, aldosterone). Different receptor zones can also be stimulated and pharmacological agents administered.

Of course, in such cases, there is only partial simulation of some elements of changes that, on the whole, are possible in weightlessness, but they can be submitted to very comprehensive analysis. Thus, one can sharply intensify some element or other, some mechanism or other of the effect on a given system or receptor field. One succeeds in obtaining vivid and distinct effects that are not as prominent in actual weightlessness [1-3].

In conclusion, it should be mentioned that none of the ground-based methods of simulating the biological effects of weightlessness can fully or adequately reproduce the real effects of weightlessness. For this reason, the final verification of facts demonstrated in model experiments and theoretical conceptions developed on their basis should be conducted in actual flights. Nevertheless, modeling may be of substantial aid in gaining understanding

of the mechanisms of effects on the organism of prolonged weightlessness. Deeper knowledge about the mechanisms of effects of weightlessness on the organism will, in turn, point to more precise routes of correcting its deleterious effects.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 612.76-06:629.78

DYNAMICS OF CYCLIC AND ACYCLIC LOCOMOTION OF THE SOYUZ-18 CREW AFTER A 63-DAY SPACE MISSION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 9-13

[Article by I. F. Chekirda and A. V. Yeremin, submitted 19 Dec 1975]

[Text] Investigation of the dynamics of locomotor activity of cosmonauts in the readaptation period is important, not only to select optimum rehabilitation measures, motor activity and physical exercise, but to evaluate the effects of long flights on the motor system. We must determine whether cosmonauts are able to perform locomotor acts after the spacecraft lands.

For this purpose, a study of locomotion was made on the crew of Soyuz-18 at different stages of the readaptation period.

Methods

Coordination of walking and jumping was studied by the method of photocyclography with recording to successive positions of parts of the body 64 times per second. Control of movements was evaluated according to parametric graphs of acceleration of movement of articulations of the leg [1]. The biomechanical parameters of walking were also studied by means of frame-by-frame analysis of filmed data. In addition, we recorded the overload curves for three coordinate axes in the projection of the arbitrary center of gravity of the body (the load sensors were placed in a backpack) and support reactions of the tips and heels of both soles (tensoliners were put in the shoes).

Bioelectric activity of anterior and posterior muscle groups of the crus and thigh was tested by the method of overall ["global"] electromyography with photographic recording. The tape feeding speed was 64 mm/s.

The cosmonauts performed the tests of walking at the rate of 120 steps/min using 0.7 m steps, with the eyes open and closed, walking at 140 steps/min using 0.8 m steps with the eyes open, maximum long jumps and high jumps from semisquatting position waving the arms forward and up. The pace was set by a metronome and length of steps were marked on the floor.

Tests were made before the mission and 2, 6 and 15 days after, on both cosmonauts, then 39 days after the flight on V. I. Sevast'yanov and 58 days after the flight on P. I. Klimuk. High jumps were tested for the first time 6 days after the flight and long jumps, 15 days after the flight, in accordance with the regimen of motor activity during the period of readaptation.

Results and Discussion

After landing, the cosmonauts were able to move independently. However, on the 1st day, visible changes in gait were noted, which disappeared entirely in 2 days. Occasionally, there was negligible, compensated loss of equilibrium. The "stamping" gait symptom observed in the crew of Soyuz-9 was not present. The foot smoothly approached the support, but it was dropped (period of "drop" gait). The changes in gait of P. I. Klimuk and V. I. Sevast'yanov were almost the same and, on the whole, were less marked than in the crew of Soyuz-9 and Soyuz-17. V. I. Sevast'yanov presented subjective sensations of discomfort while walking for 3-4 days and P. I. Klimuk did so for 6-7 days.

Unlike the crew of Soyuz-17, on the 2d day they were already able to perform at the specified walking parameters with satisfactory accuracy. Maximum deviations were present when walking with the eyes closed. They retained the capacity to walk rapidly. Both cosmonauts demonstrated underestimation of walking parameters, which resulted in moving at a faster speed than specified. Even 6 days after landing, the cosmonauts walked at a faster pace and took longer steps. P. I. Klimuk performed the specified walking test more accurately than V. I. Sevast'yanov.

The increase in pace, length of step and speed of movement was associated with an increase in vertical movements of head, hip, knee and ankle joints. The maximum values of speed increased on graphs of longitudinal and vertical components thereof. There was no appreciable change in configuration of speed curves.

The graphs of longitudinal components of acceleration of the ankle joint, reflecting control of structure of movements by the central nervous system, illustrate the main waves determining the structure of the act of walking. However, at the moment of pushing away from the support, when leg elements prepared for extensor movements in the period of carrying and stopping the leg before standing on it, additional correction waves were demonstrated. Such complication of movement structure was also present in the crews of Soyuz-9 and Soyuz-17, but in a more marked form. The structure of movements was biomechanically more purposeful in P. I. Klimuk than V. I. Sevast'yanov, and it was simpler in the latter than after his first flight.

Bioelectric activity of the leg muscles of cosmonauts increased significantly while performing the postflight specific walking tests. The periods of muscular activity and duration thereof in different phases of walking corresponded to the time of development of the main and correction waves on the

parametric graphs of acceleration of movement of leg articulations. The more complicated structure of walking was reflected in the increased frequency and duration of periods of muscular activity during the walking cycle.

Figure 1A illustrates the dynamics of averaged amplitude of electromyograms of the four main groups of leg muscle per walking cycle, in relation to the individual background taken as the unit, for the crew of Soyuz-17 and Soyuz-18. During the readaptation period, the index of intensity of muscular activity showed a 1.92-fold increase after 2 days in P. I. Klimuk, 2.4-fold increase in V. I. Sevast'yanov, 1.94-fold increase in A. A. Gubarev and 2.2-fold increase in G. M. Grechko. It should be borne in mind that the crew of Soyuz-18 exceed the specified parameters of walking and speed of movement, while the crew of Soyuz-17 could not reach the specified parameters and developed a movement rate that was slower than specified, i.e., the latter required less muscular exertion. On a comparative basis, the values of this index after 6 days, when the difference in reproduction of specified parameters leveled off, were more demonstrative.

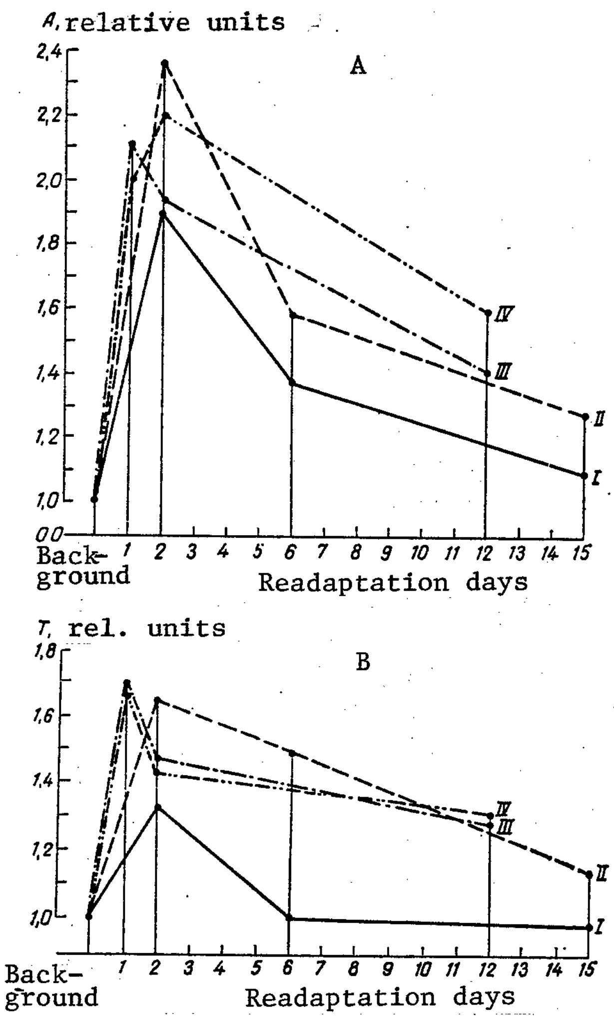

Figure 1.
Overall index of intensity (A) and duration (B) of bioelectric activity on EMG of anterior and posterior muscle groups of the crus and thigh during a cycle of specified walking at the rate of 120 steps/min with the eyes open, in relation to individual preflight levels in cosmonauts of Soyuz-17 and Soyuz-18 during the readaptation period.

I) P. I. Klimuk
II) V. I. Sevast'yanov
III) A. A. Gubarev
IV) G. M. Grechko

The index of intensity of muscular activity diminished sharply in V. I. Sevast'yanov (to 1.6), but it was higher than in P. I. Klimuk (1.37). In the crew of Soyuz-17, it constituted a mean of 1.87 and in that of Soyuz-18, 1.57. After 12 days, the index of intensity of muscular activity was also higher than before the flight. After 15 days of readaptation, P. I. Klimuk performed the walking test with less muscular exertion than V. I. Sevast'yanov.

Recovery of indices of muscular activity was better in the crew of Soyuz-18 than Soyuz-17 (Figure 1B). After 6 days, the index of duration of muscular activity did not differ from the background value in P. I. Klimuk; it constituted 1.5 in V. I. Sevast'yanov and dropped to 1.15 only after 15 days. Changes in structure of movements persisted for a longer time in both cosmonauts and were more marked in V. I. Sevast'yanov, who still complained of pain in the muscles during active movement after 15 days.

Performance of jumps required application of maximum exertion of an explosive nature. After 6 days, the cosmonauts made single high jumps from a standing position. We failed to observe visible changes in coordination. The cosmonauts complained of weakness of leg muscles. During the jump, elevation of the center of gravity diminished by 10 cm in P. I. Klimuk (by 23.8%) and 15 cm in V. I. Sevast'yanov (47.6%).

Figure 2 illustrates the deviations (expressed as percentages) from individual background values of length of jump, elevation of center of gravity of the body and overloads in the body's center of gravity along the vertical axis after 15 days of readaptation of the crew of Soyuz-18.

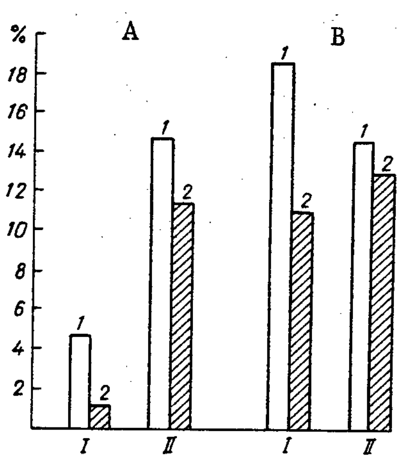

Figure 2.
Changes in metric and force characteristics of jumps made by P. I. Klimuk (A) and V. I. Sevast'yanov (B) on the 15th day of the readaptation period (% of background value)

I) long jump
II) high jump
1) length (height) of jump (meters)
2) occurring acceleration

While the magnitude of developed acceleration [overload] characterized the force component of the jumps, the height and length of the jumps also determined coordination of movements. The acceleration diminished by 1% in P. I. Klimuk during the long jump and by 11.4% in the high jump. The length of the jump diminished by 4.5% and elevation of center of gravity of the body decreased by 14.6% while jumping. V. I. Sevast'yanov did not perform the

jumps as well. The accelerations decreased by 11 and 12.5%, respectively, and the metric indices, by 18.4 and 14.3%.

After 30 days, the accelerations were 6.2 and 7.1% lower than background levels in V. I. Sevast'yanov; his metric indices were 8.1 and 7% lower. In P. I. Klimuk, the indices failed slightly to reach normal after 58 days (by 1 and 4.4% for accelerations and 2.2 and 4.1% for metric indices).

The decreased accuracy of complying with specified parameters of walking, more complicated coordination structure of movements, increased duration and intensity of muscular contractions within the walking cycle characterized discoordination of locomotor activity and worsening of the functional state of the neuromuscular system. The specified movements were performed satisfactorily, there being a tendency to underestimate the parameters. With the eyes closed, the locomotion disturbances increased more than before the flight, which is an additional indication of the increased role of remote receptors in controlling movements and transmitting to the external element of movement control the functions of the internal element, that are not inherent in the former [2].

During the readaptation period, the external features of movements were the first to recovery, then followed the biomechanical parameters of locomotion due to a more complex coordination structure of movements and intensification of muscular activity [3]. Fifteen days were not enough for recovery of impaired coordination relations. In ballistic locomotion, discoordination of movements was associated with appreciable inadequacy of the force component. Incomplete recovery of acyclic locomotion was noted after 39 days in V. I. Sevastyanov and after 58 days in P. I. Klimuk. However, it should be borne in mind that the scope of physical training was greater before the flight than after.

Inflight use of locomotion in the course of physical training on a complex physical trainer and bicycle ergometer diminished locomotor disorders, as was previously demonstrated with reference to hypokinesia [4, 5]. In spite of the fact that the Soyuz-18 mission lasted twice as long as the one on Soyuz-17, the changes in locomotor activity were less marked and recovery took less time in P. I. Klimuk and V. I. Sevast'yanov. It should be assumed that, in the case of missions lasting up to 2 months, the condition of locomotor activity in the readaptation period is determined primarily by the quality of physical exercise onboard the spacecraft and less by the duration of the mission. Furthermore, we should mention that locomotor activity was better in P. I. Klimuk than V. I. Sevast'yanov, and that the latter presented less discoordination in walking after the mission on Soyuz-18, as compared to his first 18-h flight, which is apparently attributable to an increase in volume, intensity and specificity of physical exercises.

The decreased functional capabilities of the neuromuscular system and discoordination of locomotion demonstrates the need to refine the system of physical exercise for cosmonauts onboard spacecraft, use of ways and means

of operational self-checking and programmed checking of physical exercise, based on estimation of parameters of the motor and cardiovascular systems. It would also be good to add game and competitive elements to cosmonaut training.

Comparative analysis of the dynamics of locomotion in the crews of Soyuz-9, Soyuz-17 and Soyuz-18 during the readaptation period revealed the beneficial effect of a sparing regiment of motor activity during the first few post-flight days on the course of recovery processes and subjective condition of cosmonauts. The regimen of motor activity, volume and intensity of physical exercise at the later readaptation stages require further investigation.

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MEDICAL SUPPORT OF THE IMMEDIATE POSTFLIGHT PERIOD FOLLOWING LONG SPACE MISSIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 14-16

[Article by L. L. Stazhadze, V. V. Bogomolov and I. B. Goncharov, submitted 5 May 76]

[Text] The scientific methodological aspects and questions of organizing resuscitation and anesthesiological care of acute, emergency states in the early readaptation period following lengthy, manned space missions constitute a pressing problem of space medicine [1-3].

There are a number of substantial and specific distinctions to emergency medical care in the case of development of life-endangering states in the immediate postflight period, and this is why it is imperative to find some scientific and organizational solutions [2, 4]. In essence, the specifics consist of the following: life-endangering, emergency conditions occur against the background of changes in the organism that are typical with long space missions and this, of course, requires corrections of the conventional ways and means of clinical practice with regard to resuscitation and anesthesiological measures; in the field, it is impossible to use some important laboratory, roentgenological and instrument diagnostic methods; rendering specialized medical care is preceded by a period during which the landed craft is sought and detected, some time is required to open the hatch and evacuate the cosmonauts from the craft. The space suit creates additional difficulties. For this reason, specialized medical care (including resuscitation and anesthesiological measures) is always delayed. Before the arrival of the search and rescue service, emergency medical care after the craft has landed can be rendered only to the extent of self and mutual help, and for this reason it depends entirely on the practical skills of the cosmonauts. Weather conditions, time of day and nature of locality have an appreciable effect on the technical feasibility of therapeutic measures in emergency conditions.

It would be impossible to develop and refine resuscitation and anesthesiological support of the immediate postflight period following prolonged missions without special research in this direction. It is deemed rather important

to accumulate facts on changes in functional state of the organism, its reserve capabilities [1, 5, 6], evaluation of resistance, as well as analysis of morbidity rate in the course of prolonged space missions [3, 7-9]. At the same time, experimental research is of substantial aid in working out systems of resuscitation and anesthesiological support in the early readaptation period. Thus, investigation of the effects of such different anesthetics as barbiturates, ketalar, sodium hydroxybutyrate, droperidol, fentalin, ether and fluothane, on the principal systems of the organism following 49-day antiorthostatic hypokinesia demonstrated convincingly the existence of a number of important distinctions beyond the framework of the well-known clinical forms of course of anesthesia.

Fluothane, which is widely used in modern anesthesiology, induced pre-collaptoid and collaptoid reactions against the background of gross disturbances of external respiratory function and metabolism. At the same time, a minimal reaction by the cardiovascular system and respiration was observed with the use of sympathomimetic anesthetics (ether, ketalar). Thiobarbiturate derivatives increase the tonus of peripheral vessels, lower the indices of cerebral circulation and microcirculation in the extremities, with severe depression of myocardial contractility. Neuroleptanalgesia was characterized by progressive tachycardia, arterial and venous hypertension and marked metabolic acidosis. Sodium hydroxybutyrate induces prolonged postanesthesia depression of external respiration, with typical metabolic changes and respiratory arrhythmia. It is quite apparent that the above-listed results of investigations must be borne in mind in selecting the type and method of anesthesia in the immediate postflight period. It is particularly important to stress that the demonstrated distinctions could be well-used to correct pre-anesthesia disturbances, and they must not be aggravated by an improperly selected anesthetic.

It is equally important to investigate the distinctions of the body's reaction to various injuries and trauma. Such changes as decrease in circulating blood volume, impairment of fluid and electrolyte balance, functional myocardial hypodynamia, dysregulation of vascular tonus, tension in the sympathoadrenal and kinin systems, decreased central regulatory mechanisms of external respiration cannot fail to have a substantial effect on the clinical course of acute, emergency conditions in the early readaptation period following long space missions [2, 4, 8, 10]. Thus, a decrease in circulation volume and tension of the sympathoadrenal system could induce more severe shock in response to minor trauma or burn. A decline of central regulatory mechanisms of external respiration is fraught with gross respiratory disorders in the presence of cerebrocranial trauma or asphyxia. Functional hypodynamia of the myocardium and dysregulation of vascular tonus are an adverse background for acute cardiovascular disturbances.

Research in these directions is only beginning. However, even now, we can anticipate the necessary changes in the systems of resuscitation care prevailing in clinical practice, if they are used in the immediate postflight period. The most important elements are as follows: the scope of infusion and transfusion therapy should be greater for a given acute state, with due

consideration of the decreased volume of circulation that developed during the mission; it is desirable to administer "substitutive" steroid therapy and use nonspecific inactivators at the very first stage of resuscitation care; ganglion-blocking agents, as well as pressor amines, should be used with great caution to avoid aggravation of dysregulation of vascular tonus; in the event there are signs of impaired external respiration, it is desirable to administer ancillary respiration or artificial ventilation of the lungs at an early time; the danger of recurrent collaptoid reactions makes it imperative to administer therapeutic measures in a slightly antiorthostatic position (with the exception of cases of cerebrocranial trauma and injury to the chest) to prevent "empty vessel spasm" in the brain and heart.

In view of the specific distinctions, the entire crew of the search and rescue service must be completely proficient in procedures of cardiopulmonary resuscitation, methods of stopping hemorrhages, and they should be able to administer preventive measures to prevent respiratory and cardiac disturbances.

Experience has shown that it is desirable to offer special classes on cardiopulmonary resuscitation at least once a year, with the participation of the medical personnel of the search and rescue service. In addition to lectures, practical classes are very beneficial, involving the use of molds with control devices to determine the effectiveness of resuscitation, as well as repeated screening of educational films.

The full scope of medical care can be rendered by specialized medical teams onboard mobile transport objects (helicopter, boat, motor vehicle), the lounges of which are outfitted as a resuscitation and operating room. The scope of resuscitation and anesthesiological care provides for administration of current types of general anesthesia, electropulse therapy, all types of perfusions, prolonged artificial ventilation of the lungs, catheterization of great vessels, arteriosection, venesection and tracheotomy. In equipping facilities, preference was given to small instruments with autonomous power sources. In view of the necessity for compactness, extensive work is being done, both experimental and clinical, to find the most informative indices for diagnostic and prognostic purposes, as well as monitoring the effectiveness and prompt correction of therapeutic measures.

Thus, in the immediate postflight period, in the case of onset of an acute state, the system of resuscitation and anesthesiological care requires further organizational and methodological refinement, based on research pursued in the course of actual space missions, model experiments and under clinical conditions.

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UDC: 629.78:612.351.1+612.411].015.348

DNA STATUS IN RAT LIVER AND SPLEEN FOLLOWING SPACE FLIGHT ON KOSMOS-605 SATELLITE

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[Article by G. S. Komolova, F. T. Guseynov, V. F. Makeyeva, I. A. Yegorov, R. A. Tigranyan and L. V. Serova, submitted 10 Nov 75]

[Text] Such important aspects of vital functions of the cell as reproduction, differentiation and growth are based on processes that develop in nucleic acids. In this regard, there are grounds to believe that disturbances referable to nucleic acid metabolism and structure play an important role in the biochemical mechanisms of effects on animals of various extreme environmental factors, including space flight factors. However, there are no data in the literature concerning the effects of long space flights on nucleic acids of animal tissues.

In this work, we submit the results of a study of the effect of a 22-day space flight on nucleic acid content and structural integrity of DNA in the rat liver and spleen.

Methods

Experiments were conducted on male Wistar rats. There were three experimental variants: I) the animals from the same batch as was involved in the flight were kept in the vivarium on a special diet; II) animals were maintained on earth under the same conditions as in flight; III) animals spent 22 days in flight on Kosmos-605. The animals were examined 1 and 26 days after the end of the experiment (3d or 2d variant). Liver and spleen tissues, extracted after sacrificing the animals, were analyzed for nucleic acid content and DNA structure (presence of DNA breaks and elastoviscous properties of supramolecular DNA). Total nucleic acids and DNA were assayed by the two-wave method, using spectrophotometry [1]. The amount of RNA was calculated according to the difference between (DNA+RNA) and DNA. The amount of nucleic acids was expressed in mg/g dry tissue weight.

DNA was isolated from tissue by the method of Kay [2] with additional deproteinization according to Marmur [3]. We determined the presence of single-stranded and double breaks according to intrinsic viscosity (η) of unadulterated and denatured preparations, respectively.

Table 1. Effects of space flight conditions on nucleic acids in the rat liver (M±m)

Experimental variant	Time after experiment, days	Content, mg/g dry wt.		η, dl/g	
		RNA	DNA	denatured DNA	native DNA
I (n=23)		44,4±0,7 (100%)	13,40±1,12 (100%)	51,3±0,02	125,3±0
II (n=12)	1	46,6±1,0	14,74±0,16 (110%) P<0,01	52,0±0,04	125,3±1,0
	26	43,9±4,4	13,21±0,48		
III (n=11)	1	38,0±1,2 (85,5%) P<0,01	13,06±0,46	50,9±0,4	126,0±0,1
	26	43,9±1,0	13,36±0,77	51,0±0,5	125,0±0,6

Table 2. Effects of space flight conditions on nucleic acids in the rat spleen (M±m)

Experimental group	Time after experim., days	Content, mg/g dry wt		η, dl/g	
		RNA	DNA	denatured DNA	native DNA
I (n=18)		50,9±1,9 (100%)	83,9±1,4	56,2±0,2	134,0±1,0
II (n=10)	1	55,8±2,4 P>0,1	87,4±2,0 P>0,05	54,2±0,6	133,4±1,0
III (n=7)	1	41,3±3,6 (81,1%) P<0,05	80,0±4,7	55,0±0,7	133,5±1,4
	26	55,3±1,0	91,8±1,5 (109,4%) P<0,01	56,2±0,3	134,4±1,4

The supramolecular structure of DNA (SM-DNA) was isolated from liver tissue by a soft phenol method [4]. We evaluated the structure of SM-DNA according to its elastoviscous properties. Elastoviscosity was measured with a capillary elastoviscosimeter as described in [4, 5].

Results and Discussion

The results of our investigation revealed that there is no change in DNA content of the liver per g dry tissue weight following the space flight, as compared to normal, whereas RNA level dropped by ≈14% (Table 1). For this reason, the RNA/DNA ratio dropped (from 3.3 in the control to 2.9 in the experiment). We observed an analogous phenomenon in the spleen (Table 2): RNA content dropped by 19%, as compared to the control, while RNA/DNA ratio dropped from 0.7 to 0.5.

As before, at the end of the recovery period the DNA content of liver tissue from animals that were on the space flight did not differ from the control, while RNA content reverted to normal (see Table 1).

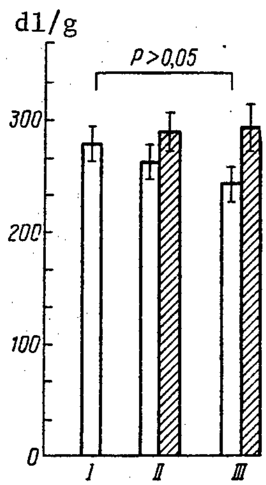
At this time, the RNA content of spleen tissue (see Table 2) also did not differ from normal, while DNA content was even slightly above normal (by ≈9%). An analogous negligible increase in DNA content of the liver was observed in the second experimental variant (see Table 1). At the same time, unlike the third variant, the second experimental variant revealed no change in RNA content of tissues of both organs examined. It should be noted that DNA content of radiosensitive animal tissues is a sensitive indicator of radiation lesion to the organism [6, 7]. Irradiation elicits a drop of DNA level in tissues. The RNA content either does not change, or drops to a considerably lesser extent than DNA. As a result the RNA/DNA ratio increases. As we have already mentioned, after the space flight, not only did this ratio fail to increase, on the contrary, it even decreased somewhat. Evidently, the decrease in RNA in the tissues examined is due to factors other than radiation. Perhaps it is related to the organism's reaction to prolonged weightlessness. In rats kept on earth (second variant) there was no change in RNA level in the tissues examined.

Chromosomal aberrations are based on unrepaired single breaks, while double breaks are responsible for cellular lethals in a number of cases.

Tables 1 and 2 show that no disturbances appeared in the organs examined that would be associated with breaks in polynucleotide chains of DNA under the influence of space flight conditions.

We tested elastoviscosity properties as another sensitive indicator of the status of DNA in the liver. This chromatin structure is an intravital element that plays an important role in cell functions [4]. One of the criteria for evaluating the condition of SM-DNA, elastoviscostiy, is highly sensitive, not only to ionizing radiation [8], but to physiological changes in the organism [9, 10].

The Figure shows that there is only a slight tendency (the data are statistically unreliable) toward decreased elastoviscosity of SM-DNA isolated from the rat liver 1 day after the space flight. This tendency disappears after 26 days. An even less marked tendency toward lower elastoviscosity of SM-DNA is observed 1 day after termination of the second experimental variant.



Elastoviscosity of SM-DNA from rat liver

I-III) experimental variants

white columns--1 day after experiment
striped columns--26 days after "

On the basis of the obtained results regarding all indices examined, it may be concluded that the disturbances observed with radiation lesion to the organism were not observed in nucleic acids of the liver and spleen of the flight experiment animals. The demonstrated negligible changes in the systems studied are reversible and functional in nature.

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EFFECT OF PROLONGED SPACE FLIGHT ON PROTEIN BIOSYNTHESIS IN VARIOUS RAT ORGANS AND TISSUES

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[Article by E. A. Rapoport, L. A. Goncharova, S. A. Morenkova and V. A. Kazaryan, submitted 16 Jan 76]

[Text]Biomedical research conducted during space flight on higher animals and man revealed various functional, as well as more profound changes in different organs and systems [1, 2]. In view of the correlation between the physiological status of cells and tissues and the course of protein biosynthesis in them [3-6], we have attempted here to study protein biosynthesis, using the method of isotope tracers, in several parenchymatous organs, the myocardium and some skeletal muscles of rats following a 22-day flight in the Kosmos-605 satellite, on the 2d and 26th days after the animals landed. This work is a part of an experiment conducted by the Institute of Biomedical Problems, USSR Ministry of Health [7, 8].

Methods

Experiments were conducted on male Wistar rats. The animals were divided into groups of 5: the 1st and 3d groups constituted the "flight" rats on the 2d and 26th days, respectively, after returning to earth; the 2d and 4th groups were rats in a synchronous experiment, which were kept in a spacecraft cabin on earth with the same life-support systems (LSS) and used on the 2d and 26th days, respectively, after removal from LSS. Four batches of intact animals served as a control; they were kept in the vivarium on the same diet. The weight characteristics of the animals are given in Table 1.

We gave all of the animals intraperitoneal injections of 2-^{14}C-leucine at the rate of 5 μCi per 250 g weight. One hour later, the rats were given pentothal anesthesia, the abdominal cavity was opened; the animals were exsanguinated by puncturing the portal vein, and samples of different organs and tissues were taken (liver, kidneys, lungs, pancreas and thymus, testes). We isolated total proteins from these tissues by the usual method [3]. We extracted proteins of sarcoplasm and myofibrillar complex according

to the system of I. I. Ivanov [9], precipitating them with trichloroactetic acid (TCA) and then washed them [3] to prepare samples for measurement of radioactivity. The protein preparations were dissolved in 0.3 n. alkali and radioactivity was determined with a precision of 1-2% on a liquid scintillation spectrometer, using Bray's fluid as the scintillation mixture. We assayed the concentration of proteins by the Lowry method [10]. In view of the fact that the level of incorporation of radioactive amino acids in protein depends not only on the actual rate of biosynthesis thereof, but on intensity of delivery of labeled precursors to cells, we made a separate determination of concentration of labeled amino acids in cells of organs and tissues studied and intensity of incorporation thereof in protein molecules. This enabled us to describe more accurately the state of protein biosynthesis. For this purpose, we obtained TCA extracts from tissues, removed TCA by repeated ethyl ether extraction and determined radioactivity by the above-mentioned method.

Table 1. Weight of animals (g) used in radioisotope experiments

Experimental animals			
"flight"	"synchronous"	"flight"	"synchronous"
2d day		26th day	
246±7	266±12	304±7	378±5
Vivarium control animals			
279±21	293±9	301±11	327±16

Note: Here and in Tables 2 and 3, the means of 5 readings are given, with the exception of specially marked cases (figures in parentheses).

Tissue homogenates were separated by the method of differential centrifugation described previously [11], in order to define the biosynthesis of proteins of different subcellular structures of the liver. The nuclei were purified by the method of Chauveau [12], then the globulin fraction, total histones and HCl-fast ("residual") proteins were extracted from them [6].

Along with investigation of biosynthesis of total proteins of the pancreas in vivo, we also made an in vitro study of insulin biosynthesis in this tissue. For this purpose, tissue slurry was incubated in bicarbonate buffer, pH 7.4, in the presence of ^{14}C-glycine with specific activity of 170 mCi/g, at the rate of ~0.1 mCi/100 mg tissue, for 30 and 60 min at 37°, in a thermostat-controlled bath, with slow rocking. After incubation, the tissue was separated from the centrifugation medium, washed twice in buffer solution containing a 100-fold excess of unlabeled glycine and frozen in dry ice. Insulin was obtained by extraction with acid alcohol [13], followed by purification by the method of isoelectric precipitation and then filtration through G-50 Sephadex.

Results and Discussion

Table 2 shows that, in most cases, there were no changes in intensity of concentration of ^{14}C-leucine in tissue cells of "flight" and "synchronous" rats. A tendency toward decreased intensity of this process was observed only in the testes of "flight" rats in the 3d group, as well as kidneys and thymus of "synchronous" rats in the 4th group.

Table 2. Radioactivity of protein-free extracts of tissues from intact, "flight" and "synchronous" rats 1 h after administration of ^{14}C-leucine (M±m)

Organs and tissues	Vivarium control	Experimental groups			
		"flight"	"synchr."	"flight"	"synchr."
		2d day		26th day	
	Counts/min/10 mg tissue				
Liver	200±19	178±9	183±14	158±20	155±6
Pancreas	1366±212	1373±71	1426±36	1185±126	1285±128
Kidneys	216±11	206±9	232±11	230±20	181±8*
Lungs	193±27	161±4	180±13	202±36	155±8
Thymus	276±20	316±88	268±18	239±22	207±15*
Skeletal muscles					
M. extensor digitorum longus	202±12	219±13	185±25	188±14	184±19
M. quadratus lumborum	153±23	164±8	176±8	169±14	147±4
Testes	183±11	165±7	167±13	139±13*	153±9

*The decline is reliable ($P<0.05$).

Table 3 shows that there was activation of biosynthesis of cardiac sarcoplasm proteins in "flight" rats, on the 2d day after returning to earth, in the absence of changes in biosynthesis of myofibrillar complex proteins. This change in metabolism of sarcoplasm proteins in "flight" rats is not, however, the results of effects of space flight factors, since an analogous change develops in animals in the ground-based synchronous experiment (2d group). In both groups of rats, the changes in biosynthesis of cardiac sarcoplasm proteins level off 26 days after termination of experimental conditions. There are no reliable changes in sarcoplasm protein biosynthesis in the quadriceps muscle of the thigh, either in "flight" or "synchronous" animals, as compared to the intensity of this process in the vivarium control. At the same time, there is a decrease in intensity of biosynthesis of myofibrillar proteins in the "flight" rats, on the 2d day after returning to earth, in the absence of reliable changes in this process in "synchronous" rats of the 2d group, which is indicative of a link between these changes and factors of space flight. At the late postflight stages, the "flight" rats also presented a decrease in biosynthesis of myofibrillar proteins. However, in "synchronous" rats as well, 26 days after removal from LSS, the intensity of this process was somewhat lower than in the vivarium control.

Table 3. Incorporation of ^{14}C-leucine in proteins of organs and tissues of control, "flight" and "synchronous" rats (M±m)

Organs and tissues	Vivarium control	Experimental animal groups			
		flight	synchr.	flight	synchr.
		2d day		26th day	
	Counts/min/mg protein				
Heart:					
sarcoplasm	152±10	191±8*	188±9*	151±7	168±12
myofibrillar complex	130±14	125±13	144±6	138±6	133±11
Lungs	258±25 (8)	237±17	259±17	269±11	284±28
Thymus	332±14 (16)	336±11	308±29	397±19*	346±25
Liver	574±42 (7)	571±37	468±51	570±31	474±54
Pancreas	2253±191 (19)	2295±227	2756±619	2322±499	2608±183
Kidneys	433±31 (12)	360±19	429±20	461±19	403±18
Testes	128±14	136±18	138±31	134±5	137±8
Skeletal muscle: (m. quadriceps femoris) Sarcoplasm:	75±10	81±5	65±6	53±6	78±4
myofibril.complex	57±4	39±4*	50±5	44±4*	42±2*

*The difference is reliable in relation to the vivarium control ($P<0.05$).

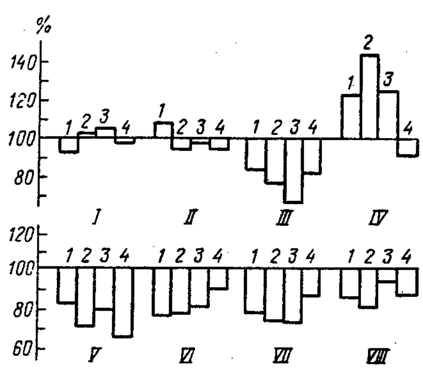

Figure 1.
Change in incorporation of ^{14}C-leucine in proteins of various subcellular structures of the liver of "flight" and "synchronous" rats. The levels are given as percentages of vivarium control. Cell fractions:

I) total cytoplasm proteins
II) mitochondria
III) microsomes
IV) cellular juice
V) total nuclear proteins
VI) nuclear juice proteins
VII) histones
VIII) "residual" nuclear proteins

Animal groups:
1) "flight," 2d day
2) "synchronous," 2d day
3) "flight," 26th day
4) "synchronous," 26th day

In the vast majority of cases, no visible changes were demonstrated in biosynthesis of total proteins in other organs of experimental animals. Only incorporation of ^{14}C-leucine in thymus proteins of the 3d group of "flight" rats was somewhat elevated; however, it did not differ appreciably from the level in the corresponding vivarium control (see Table 1).

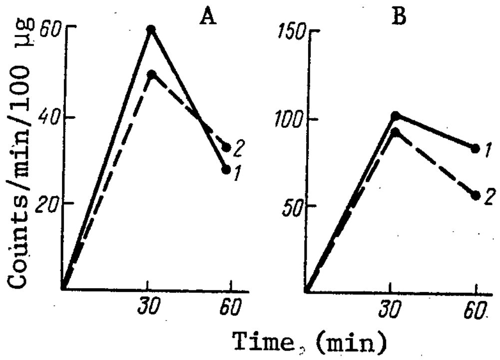

Figure 2.
Incorporation of ^{14}C-glycine in insulin of pancreas slurry from intact (vivarium) and flight rats

A) 2d postflight day
B) 26th postflight day
1) intact rats
2) "flight" rats

While the study of incorporation of ^{14}C-leucine in homogenate proteins (see Table 3) and total proteins of liver cytoplasm (Figure 1) failed to demonstrate changes in biosynthesis thereof in "flight" and "synchronous" rats, a separate study of subcellular fractions revealed typical changes. Thus, while there was no change in radioactivity of mitochondrial proteins 1 h after administration of ^{14}C-leucine, the radioactivity of microsomal proteins of "flight" rats and, to a somewhat lesser extent, in "synchronous" animals was low, while that of proteins of cell juice was high; the radioactivity of total nuclear proteins and fractions thereof was also low in "flight" and "synchronous" rats. The possibility cannot be ruled out that, along with changes in biosynthesis, this could be a reflection of altered exchange of de novo protein molecules between different cellular structures.

As is the case with biosynthesis of total proteins, there are no appreciable changes in rate of insulin synthesis in the pancreas (see Table 3) after the "flight" animals returned to earth (Figure 2), which is indicative of resistance of the insular system to the effects of space flight factors.

The results of these studies warrant the conclusion that a 22-day space flight does not elicit any specific changes, in most of the organs studied, in biosynthesis of proteins that are not present in the synchronous ground-based experiment under comparable life-support conditions. This is indicative both of good adaptation of the rat organism to flight conditions and effectiveness of LSS function. An appreciable difference is, however, observed in the response referable to skeletal muscles, with prevalence of white fibers, namely the femoral quadriceps, in which weightless and diminished function depress biosynthesis of myofibrillar proteins. Typically enough, the changes in metabolic activity of proteins, demonstrable in some of the organs we examined, disappear at a dissimilar rate in the course of adaptation to the usual living conditions: changes in metabolism of proteins of the liver, on the subcelluair level, persist to the end of our observation period, whereas they already disappear in the myocardium.

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CYTOCHEMICAL STUDIES OF PROTEINS AND RNA IN INDIVIDUAL SPINAL CORD MOTONEURONS AND SPINAL GANGLIA NEURONS OF RATS FOLLOWING A SPACE FLIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 24-28

[Article by A. V. Gorbunova and V. V. Portugalov, submitted 10 Oct 75]

[Text] It should be considered established that weightlessness leads to functional changes in the motor analyzer [3]. However, the question of the extent to which they affect metabolism of neurons of different cellular elements of the analyzer has not yet been investigated comprehensively. Weightlessness is associated with a significant decrease in load on the skeletomuscular system and, according to several authors [2, 4, 5], this leads to development of signs of muscular atrophy. It is a known fact that motor and sensory innervation affects trophic processes in muscles [9, 21]. The link between neurons and innervated tissues is maintained by means of constant reception and transmission of information, which has a considerable effect on trophics of both the innervated and innervating substrates. There are grounds to believe that the structural integrity of a neuron is related to its connection with innervated organs. Since weightlessness is associated with changes in activity of the motor analyzer and leads to atrophic changes in muscle tissue, it was interesting to investigate the metabolism of motoneurons of the anterior cornua of the spinal cord and neurons of the spinal ganglia contained in the spinal reflex arc, in which the neurons of the spinal ganglia play the role of afferent structures, while the motoneurons of the anterior horns play that of efferent structures. Changes in RNA and protein content in the presence of diverse physiological loads could be one of the indicators of functional activity of neurons.

The objective of this work was to study changes in RNA and protein content of motoneurons of the anterior cornua of the spinal cord and sensory neurons of spinal ganglia of rats used in a 22-day space flight. Rats kept in the vivarium and used in a ground-based model experiment, in which most of the factors of space flights were simulated, served as controls.

Methods

We took the spinal cord with adjacent ganglia on the level of the lumbar thickening from control and experimental animals 1 and 27 days after the

flight. Samples of spinal cord, 2-3 mm in thickness, and spinal ganglia were fixed in Carnoy fluid and imbedded in paraffin. Motoneurons of the anterior cornua of the spinal cord and sensory neurons of spinal ganglia were isolated from 40 μm sections with a Von Bruhn micromanipulator under MBI=3 microscope monitoring. In order to assay RNA content of individual neurons, we used the micromethod described by Edstrom [18] and modified by L. F. Maksimovskiy [8]. We calculated the RNA content of an individual cell by the method of Slagel and Edstrom. Dry weight of cytoplasm of spinal cord motoneurons and cytoplasm of spinal ganglia neurons was determined by interferometry in sections 7 μm thick. Measurements were made with a two-beam interference microscope of the Leitz Company, with a 50× objective and 10× ocular. We used the following formula to assay dense substances in the cell:

$$P = \frac{\Delta\delta \cdot S}{\alpha \cdot 100}$$

where P is dense substance content, g; $\Delta\delta$ is optical difference in path, cm; α is specific coefficient of refraction of the object, which equals 0.0018±2% for protein substances, and S is the area of the structure examine, cm^2.

All the digital material was submitted to processing by methods of variation statistics.

Results and Discussion

Examination of spinal ganglia neurons and motoneurons of the anterior cornua of the spinal cord yielded information on some cytochemical characteristics. We distinguished three categories of neurons in the spinal ganglia, which differed in size and other parameters. We made a separate study of small, medium and large neurons. It was established that different groups of neurons react differently. Table 1 shows that a 22-day space flight was not associated with changes in RNA content of medium and small neurons of the spinal ganglia. We demonstrated a distinct decline (by 13%) in RNA content of the bodies of large neurons. We failed to observe reliable differences between the three categories of neurons in experimental and control animals 24 days after landing. After the flight, the protein level of cytoplasm of medium and small sensory cells remained unchanged. In large neurons, we found a decrease (by 14%) in protein content of cytoplasm of the cells examined, and it remained low (11%) 27 days after landing (Table 2). Experiments conducted on the ground were not associated with reliable changes in RNA and protein content of the bodies of the neurons examined.

Examination of motoneurons of the anterior cornua of the spinal cord of experimental rats failed to demonstrate reliable changes in RNA content 1 day after the 22-day space flight. On the 27th postflight day, a reliable 19% increase was demonstrated in RNA content of the bodies of the neurons (Table 3). The 22-day space flight was associated with a reliable, 19% decrease in protein content of the neurons examined, but it reverted to the normal level after 27 days (Table 4). Model experiments were not associated

with reliable changes in cytoplasmic protein and RNA content of the neuronal bodies (see Tables 3 and 4).

Table 1. RNA content (pg) of neurons of spinal ganglia of rats following 22-day space flight

Time	Cells		
	large	medium	small
1 day after flight	760±23*	545±24	193±18
1 day after ground experim.	873±40	467±28	170±12
27 days after flight	853±31	482±24	232±16
27 days after ground experim.	875±39	480±31	194±10
Control	873±15	501±15	196±7

Notes: 1. Each mean RNA level per cell was obtained from the results of analysis of 90-280 cells taken from 3-14 animals.

2. The asterisk refers to a reliable difference, in relation to the control ($P<0.002$).

Table 2. Protein content (pg) of neuronal cytoplasm in spinal ganglia of rats following 22-day space flight

Time	Cells		
	large	medium	small
1 day after flight	1708±116*	960±45	492±31
1 day after ground experiment	1800±96	1133±61	503±32
27 " " flight	1771±85*	1091±94	447±21
27 " " ground experiment	1956±64	1022±41	440±11
Control	1980±45	1025±25	472±14

Notes: 1. The asterisk refers to a reliable difference, in relation to the control ($P<0.05$).

2. Here and in Tables 3 and 4, each mean value was obtained from the results of analyzing 90-360 cells taken from 3-12 animals.

Table 3. RNA content (pg) in motoneurons of rat spinal cord after 22-day space flight

Control	After space flight		After ground experiment	
	1 day	27 days	1 day	27 days
515±8	516±11	616±16*	490±21	485±19

Note: The asterisk refers to a reliable difference, in relation to the control ($P<0.001$).

Table 4. Protein content (pg) of motoneuron cytoplasm in spinal cord of rats after 22-day space flight

Control	After space flight		After ground-based experiment	
	1 day	17 days	1 day	27 days
2163±56	1772±82*	2277±152	2205±91	2197±115

Note: The asterisk refers to a reliable difference, in relation to the control (P<0.002).

Motor function disturbances develop during space flight [3, 5]. One of the factors determining these disturbances is the decreased flow of information (proprioception) from somatic muscles, as a result of low functional load and relaxation of antigravity muscles. The shortage of proprioceptive impulsation can probably create "deficient excitation" in nerve centers and thereby alter the normal reflex and trophic processes in them [7]. The level of proprioception modulates metabolism in neurons of the motor analyzer, adapting it to the organism's living conditions. Neurons, which are deprived of normal access of afferent signaling from proprioceptors for some reason or other, are subject to partial or complete atrophy [17]. Barron [16] observed chromatolysis and marginal localization of the cell nucleus in motor cells of the anterior cornua of the spinal cord after transection of posterior radices in monkeys. L. A. Pchelina [10], who severed the posterior radices, observed a change in synapses of motor cells of the spinal cord and decrease in size of motoneurons. I. I. Rampan [11, 12], in experiments involving resection of spinal ganglia, demonstrated chromatolysis in motoneurons of the anterior cornua. We demonstrated a decrease in protein content of motoneuron cytoplasm, as well as RNA and protein content in the cytoplasm of large sensory neurons 1 day after a 22-day space flight. Evidently, the decrease in protein and RNA content of the neurons examined can be evaluated as changes implementing adaptation to new conditions: lower level of motor function. At the present time the significance of the role of protein and RNA synthesis is quite recognized with regard to onset of adaptive reactions of the organism [6].

In all likelihood, the observed changes in metabolism of proteins and RNA of nerve cells can be related not only to their function, but humoral influences associated with this function, i.e., effects of hormonal stressors. In this case, the change in concentration of croticosteroids of blood plasma could lead to changes in RNA and protein content of neurons. This appears likely, since there is information in the literature concerning the effect of stress on metabolism of proteins and nucleic acids in nerve tissue [13-15, 20]. Intensified disintegration of RNA and proteins of cytoplasm, as well as slower renewal of proteins and RNA in the neurons examined could be the mechanisms that lead to a decrease in protein and RNA content of nerve cells.

Upon returning to earth's gravitation, which becomes a stronger stimulus of the gravireceptor system of muscles after adaptation to weightlessness,

there is an increase in impulsation, and this is perhaps the cause of higher RNA level in nerve cells of rats 27 days after the space flight. Evidently, accumulation of RNA in the neuron is due to intensified RNA synthesis, and it is a reflection of the compensatory reaction of the biosynthetic system of the nerve cell to the decrease in cellular proteins. In this case, according to F. Jacob and J. Monod [1], the decrease in amount of proteins acting as a repressor could elicit marked derepression of the corresponding DNA Locus, on which RNA is synthesized. As a result, the RNA level rises in the cell. Only after this does protein synthesis begin, as a result of the template coding role of RNA in biosynthesis of protein macromolecules. The increased protein content in neurons on the 27th postflight day confirms these views.

These investigations showed that a 22-day space flight does not alter RNA content of motoneurons of the anterior cornua of the spinal cord, but does elicit a decrease in RNA content of large sensory cells of spinal ganglia. There was a reliable decrease in proteins of cytoplasm of motoneurons and neurons of spinal ganglia, as compared to the control level. On the 27th postflight day, there was a reliable increase in RNA content of motoneurons of the anterior cornua of the rat spinal cord, while the RNA content did not differ from the control in sensory cells of spinal ganglia. On the 27th postflight day, the protein content of motoneuron cytoplasm returned to the initial level, while it remained low in the cytoplasm of large sensory neurons of spinal ganglia. The demonstrated dynamic differences in RNA and protein content of motoneurons of the anterior cornua of the spinal cord and neurons of spinal ganglia are, apparently, one of the manifestations of differences in metabolism of afferent and efferent systems.

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VESTIBULOTONIC REFLEXES IN MUSCLES OF THE RAT HIND LIMB FOLLOWING A FLIGHT ON KOSMOS-605

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 28-34

[Article by Z. I. Apanasenko, submitted 2 Aug 76]

[Text] The objective of this work was to study the changes in characteristics of vestibulotonic reflexes in skeletal muscles of animals under the influence of space flight conditions. According to the classical experiments of Magnus, such a reflex originates in the sensory utricular maculae when there is a change in spatial position of the body. Thus, the changes in parameters of the reflex should reflect, to some extent, the functional state of the vestibular analyzer, and mainly of its otoliths [1].

Methods

Electromyograms were recorded using silver plate electrodes on the group of femoral extensor muscles. The electrodes, mounted in a thin plastic plate, were attached to the limbs with adhesive tape. A special device was used to integrate action currents of muscles concurrently with the ink tracing on paper; total electric activity was expressed in relative units on electronic counters. We recorded bioelectric activity of muscles for 3 successive 10-s periods: at rest, with adequate stimulation of the vestibular system and immediately after such stimulation. The paper tracing also enabled us to calculate the latency period and aftereffect time of the reaction to the vestibular test.

We used measured swinging of the animal about its longitudinal body axis on a special device, for 10 s at a frequency of 0.6 cycle/s and inclination of 25°, as an adequate stimulus of the vestibular system. In each experiment, the test swinging was repeated 3-5 times to determine the variability of the results obtained.

During the experiment, the animal was kept in a plastic chamber that restricted movement and allowed it to maintain a natural seated position.

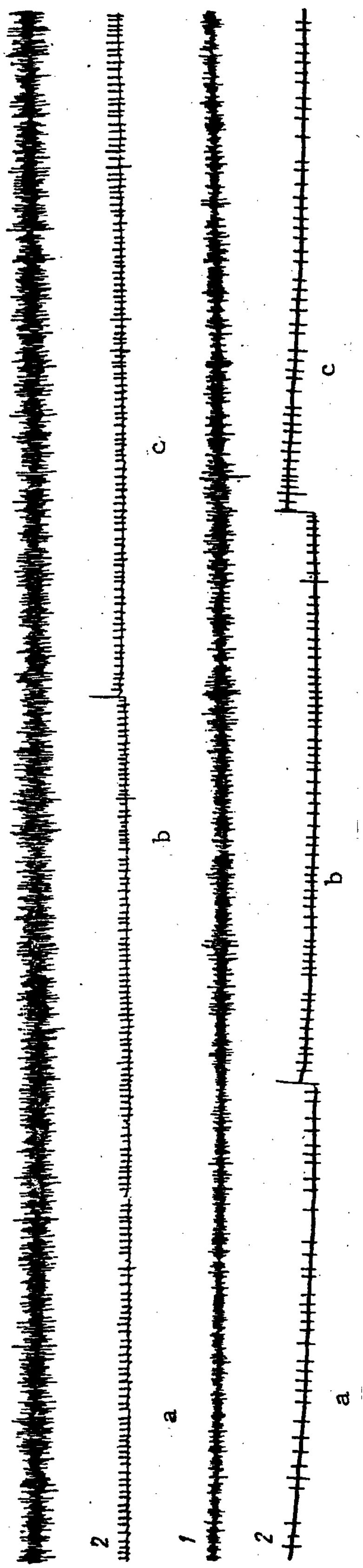

Figure 1. EMG of hind limb muscles of control group of rats. Here and in Figure 2: a) relative calm b) adequate stimulation of vestibular system (swinging) c) aftereffect of this stimulus 1) EMG 2) tracing to electronic counter after integrat.

At specific intervals after the flight and synchronous experiments, we examined three groups of animals four times: those involved in the main experiment, the synchronous group and laboratory control. Each group consisted of 13-16 male rats of about the same weight and age. The parameters studied were recorded on the 2d-4th, 14th-15th and 23d-24th days after completion of the corresponding experiments.

We used the criteria of Student, Fisher and Man-Whitney for statistical processing of the data. In some cases, they were checked by the median test.

Results and Discussion

As a rule, the electromyograms (EMG) in a state of relative rest (Figure 1) constitute rather uniform oscillations of potential with an amplitude of 20-100 μV. During test swinging, periods of increased electric activity usually appear on the EMG (amplitude of 70-300 μV). The aftereffect of the reaction to adequate vestibular stimulation is manifested either by 2-3 periods of increased electric activity, or uniform increase in amplitude of action currents of muscles to 60-200 μV. Quite often there is no distinct aftereffect.

As a result of analyzing the EMG and digital indices, some differences were demonstrated between the groups of animals. There is a general trend of decreased electric activity in rats involved in the flight and, to a lesser extent, in the group of animals in the synchronous experiment. The most marked depression of myoelectric activity was demonstrated in the flight experiment animals at relative rest. The EMG is appreciably depleted with marked decrease in amplitude of action currents. In some cases there was virtually no spontaneous impulsation (with the amplification level used) (Figure 2).

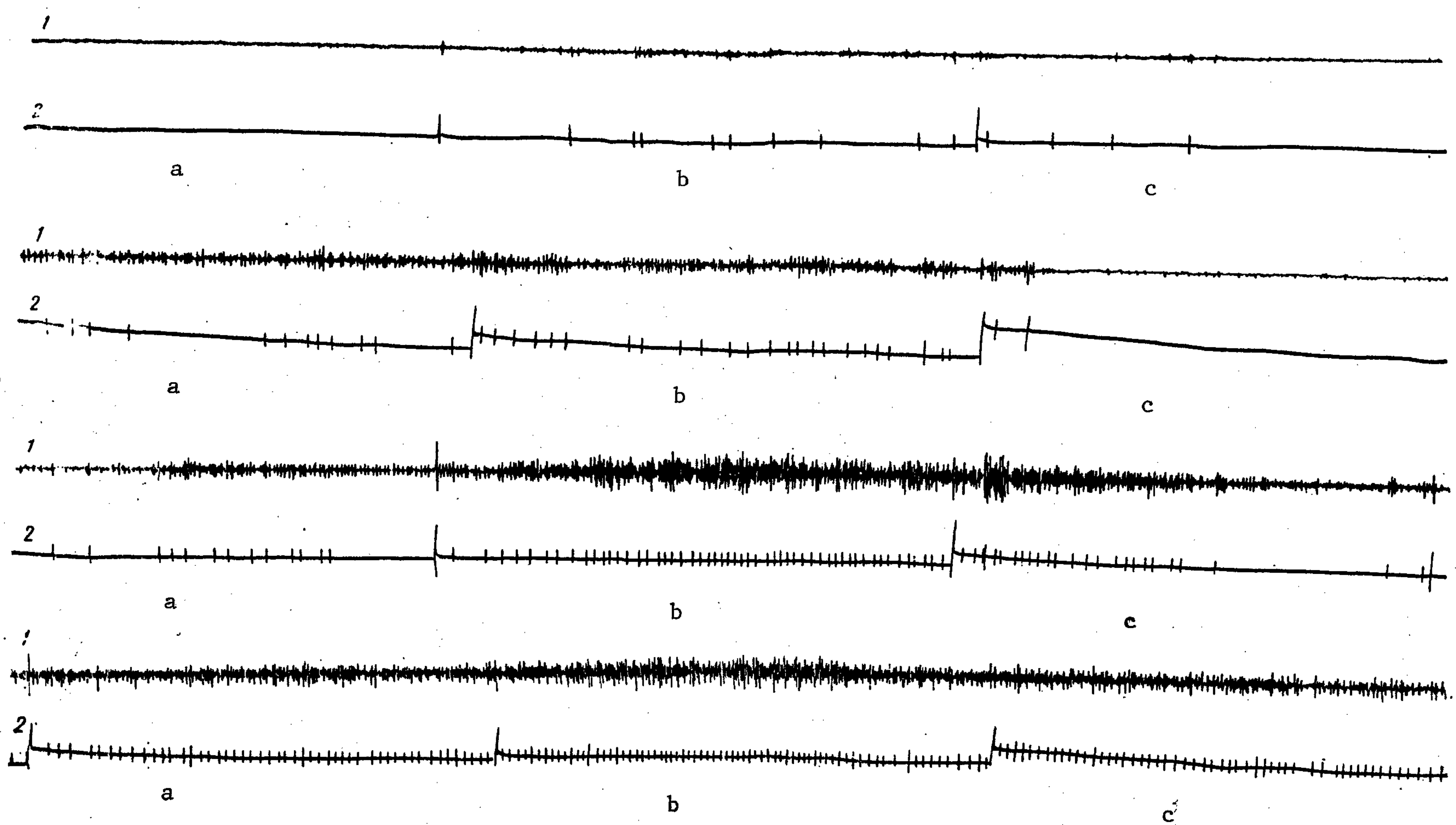

Figure 2. EMG of hind limb muscles of rats following flight on Kosmos-605 satellite.

We see a decrease in electric activity of muscles followed by partial or complete restoration. An instance of severely decreased bioelectric impulsation in the aftereffect of the vestibulo-tonic reaction is also illustrated.

This phenomenon is the most typical at the early stages of the study (Figure 3, test I). The level of spontaneous electric activity of muscles increases 1-2 weeks after the flight (test II and particularly III) and is close to the laboratory control. However, after 3 weeks (test IV), there was a second wave of decrease in spontaneous electric activity of muscles in the main experimental group of animals, and this was not observed in the synchronous experiment. As we have already indicated, the changes in the synchronous experiment group presented essentially the same direction as the flight experiment, but they were less marked. Statistical processing of the results showed that this was manifested by the fact that the changes in spontaneous electric activity of muscles in the group of animals in the synchronous experiment were statistically unreliable at all tested times, whereas the corresponding changes in flight animals differed reliably from the laboratory control in the 1st and 4th tests ($P<0.01$ and <0.05, respectively).

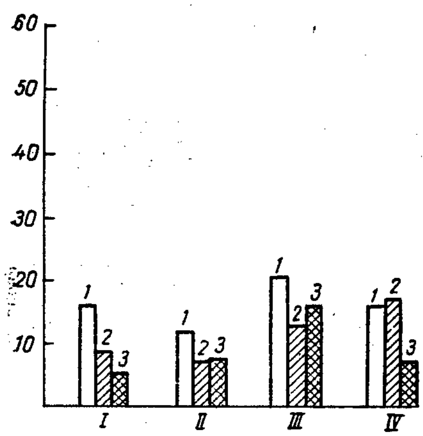

Figure 3.
Mean level of spontaneous electric activity of hind limb muscles of rats in compared groups at different times.
Here and in Figure 4:
1) control group
2) synchronous experiment
3) flight group
I-IV) examination on 3d-4th, 5th-6th, 14th-15th and 23d-24th days, respectively, after end of experiment. Bioelectric activity is expressed in integrated relative units of the electronic counter

There was also some decrease in electric activity of muscles of experimental groups of animals (as compared to the laboratory control) during the period of adequate stimulation of the vestibular system. At this time, the EMG was somewhat lower in amplitude and frequency than in intact animals in the laboratory control (see Figures 1 and 2). However, the electromyographic expression of the reaction to test swinging, even in absolute indices, was less decreased than the level of spontaneous electric activity at rest. Interestingly enough, the decrease in myoelectric acitivity in the flight group of rats was even less marked (with the exception of the 4th test) than in the animals in the synchronous experiment. But if we evaluate the bioelectric response of muscles to the vestibular test as a percentage of level of spontaneous electric activity of muscles in each instance, we find a significant increase in muscular response to stimulation of the vestibular system (Figure 4). The fact that the increase in vestibulotonic reactions occurs only in the main experimental groups of animals is remarkably distinct. In the synchronous experiment group, these reactions were very similar to those of the laboratory control animals, and did not differ

reliably from the latter (P<0.05). But the changes in postflight animals were undulant and reliable in the 1st (P<0.05) and 4th (P<0.01) tests.

In the aftereffect of the reaction to stimulation of the vestibular system, electric activity was appreciably diminished in test I in both experimental groups of animals, in test III in the synchronous experiment group and in test IV in the flight group. However, with recalculation of electric activity of muscles in the aftereffect of vestibular stimulation in relation to the level of spontaneous impulsation, we observed findings similar to those during stimulation proper ("reaction"). Muscular electric activity in the aftereffect period did not differ essentially from the laboratory group in the group of the synchronous experiment (with the exception of perceptible, but unreliable decrease in test I). But the animals in the main experiment present 2 waves of statistically reliable increase in myoelectric activity: in the 1st (P<0.05), 3d and 4th tests (P<0.01).

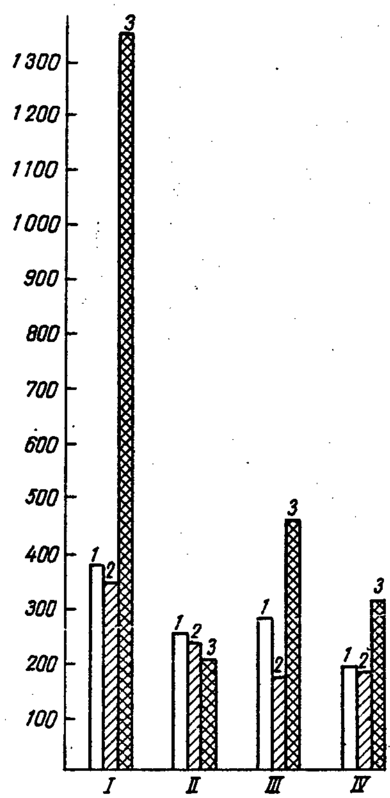

Figure 4.
Mean electric activity of hind limb muscles of compared rat groups during stimulation of vestibular system by swinging. The reaction level is expressed as percentage of spontaneous electric activity

Specific examples of EMG tracings of the vestibulotonic reaction (see Figures 1 and 2) show outwardly (unrelated to spontaneous) decreased electric activity of muscles of animals in the experimental group, as compared to the control. In addition, we see different forms of expression of the aftereffect. It must be noted that, in rats, the bioelectric expression of aftereffect of the vestibulotonic reaction is very variable, it often stops unexpectedly or is not manifested at all. A comprehensive analysis of the obtained data revealed that more or less significant deviations from the control are observed in both experimental groups of animals. However, these changes were somewhat different in quality and more substantial in the main experimental group.

The longer duration of the observed deviations is also indicative of more profound changes in these animals. In this respect, there were overtly phasic changes; usually a second, somewhat smaller wave of changes in virtually all indices is observed at the third and fourth examination. Thus, even by the 24th postflight day, we cannot report total normalization

of the parameters tested. By this time in the synchronous experiment, the indices are very close to control levels. The impression is gained that, because of less severe deviations in the synchronous experiment group, there is gradual normalization of characteristics; the second wave does not develop at these times.

It may be assumed that one of the substantial causes of decreased electric activity of muscles was some weakening of the muscles due to relatively limited movement under the conditions of both experiments. In the flight experiment, this restriction of mobility was apparently aggravated by the effect of weightlessnes, which led to more profound changes.

A decrease in electric activity of muscles was observed both before and during adequate stimulation of the vestibular system. However, the electromyographic expression of the reaction to test swinging was relatively less decreased than the level of electric activity at rest. Evidently, this is indicative of the fact that the observed decrease in electric activity of muscles is determined primarily by the condition (weakening) of the muscular effector system. However, in the system of the vestibular analyzer, after the main experiment there was prevalence of excitatory processes, which were the cause of accentuation of the actual vestibulotonic reaction and its aftereffect (as percentage of spontaneous electric activity) in the flight group of animals. We recorded similar signs of persistent excitation in the system of the vestibular analyzer previously in guinea pigs after a 24-h orbital flight on the second artificial satellite [2]. Apparently, due to the shortness of that flight, we did not observe an absolute decrease in bioelectric activity of muscles, either at rest or during a vestibular test.

Most probably, accelerations, particularly during the descent, were the cause of the rather persistent excitatory focus in the system of the vestibular analyzer. We observed prolonged elevation of the electromyographic component of vestibulotonic reactions repeatedly under laboratory conditions with the use of a centrifuge [3]. In addition, the sensitivity of the vestibular analyzer to subsequent accelerations could have been increased under the influence of prolonged weightlessness. Evidently, reactions of a readaptation nature following prolonged weightlessness could also be of some significance. The lack of accelerations in the synchronous experiment rules out the possibility of singling out the role of weightlessness from the set of factors that affected the functional state of the vestibular analyzer in that flight. Evidently, the changes were primarily of a functional and reversible nature, and they were not associated with appreciable changes in analyzer activity.

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UDC: 612.592.1+612.821].017.2(99)

CLINICAL AND BIOCHEMICAL ASPECTS OF HUMAN ADAPTATION TO CENTRAL ANTARCTICA AS APPLIED TO PROBLEMS OF SPACE BIOLOGY AND MEDICINE

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[Text] Human adaptation to deleterious environmental factors is one of the principal problems of modern biology and medicine. In the last few years, scientists have become increasingly concerned with research on these factors under natural conditions as an adjunct to investigation of human adaptation to extreme conditions [1-3].

In this work, an effort was made to use the conditions prevailing in central Antarctica for this purpose. Spending a winter at the Vostok station, with prolonged isolation of a group of individuals, the hazard, unique biological rhythms and effects of other extreme factors, is very similar to a space flight.

Methods

Table 1 lists the main parameters of climatic conditions at the Vostok station during the 17th Soviet Antarctic expedition. From November 1971 to December 1972, comprehensive examinations were made of the polar explorers, paying special attention to the nervous system. The motor system was studied by the method of medical and physical culture monitoring. Examination of the cardiovascular system involved recording of the EKG in 12 leads with the Master double [two-step] test (in the 1st, 3d, 5th, 7th and 10th min) and 20-min active orthostatic test. Before, during and after the postural test, we recorded the pulse rate, EKG in 12 leads, measured arterial pressure by the Korotkov method, performed the breath-holding functional test, cutaneous thermotopometry and tested digital tremor using a tremograph. We evaluated the psychological status of the explorers by means of daily, detailed entries in logs, which took into consideration the distinctions of behavioral reactions of each member of the group and interpersonal relations.

Hemopoiesis was studied using the conventional methods [4, 5].

The entire group at the Vostok station (27 people) was submitted to a comprehensive examination. It consisted of men 25-47 years of age, who had undergone a special medical work-up prior to the expedition and were deemed in good health and fit for spending a year under the rigorous conditions of central Antarctica. Thirteen of them were participating in an expedition for the first time (1st group), and the other 14 had participated previously in analogous expeditions to Antarctica or Arctica (2d group). The different systems were submitted in turn to examination at the intracontinental Vostok station. Each cycle of tests was usually repeated monthly at the same times.

Results and Discussion

Reorganization of the dynamic stereotype of the expedition members was associated with diverse changes in higher nervous activity, with worsening of physical condition and appearance of diverse algesic sensations (headache, painfulness referable to the heart, muscles, joints, etc.). During the first week at the station, all of the subjects presented symptoms of altitude sickness: headache, dyspnea at rest, cyanosis of the lips, dry mucous membranes, palpitations, dazed [or deafness] feeling, weakness and vertigo. About 1 month later, the acute symptoms gradually leveled off, only dyspnea remaining, which appeared when moving and experiencing a physical load. In the 2d group of explorers, the acute period of acclimation was shorter and subjectively much milder. In the overall structure of morbidity during the first stage (January--March) there was prevalence of trauma and acute respiratory disease. The course of traumatic and wound processes became extremely protracted.

In the second stage of the expedition (April--May), the number of traumas and acute respiratory diseases diminished sharply. With onset of polar night, many of the individuals began to develop signs of the asthenoneurotic syndrome. There were exacerbations of a number of diseases (essential hypertension, chronic tonsillitis, otitis, cholelithiasis), which had been compensated or undiagnosed prior to the expedition.

At the third stage (July--September) of the expedition, there was appearance of pustular pathology of the skin and subcutaneous cellular tissue (3 cases of furunculosis and 1 of suppurative lipoma). With onset of polar days, more work was done out of doors and we again observed pathology based on cooling: acute sore throat, neuromyositis, exacerbation of chronic lumbosacral radiculitis.

There were signs of the asthenoneurotic syndrome in 15 cases, most often among those who were in Antarctica for the first time. These signs appeared in some individuals toward the end of the first stage of the expedition. As the last aircraft departed, there was a visible decrease in general activity, the explorers became more introverted and melancholic. Two men developed marked signs of neurotization: irritable weakness, variability

Table 1. Main characteristics of climate at the Vostok station during the period of the 17th Soviet Antarctic expedition

Parameters	Month											
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
Air temp., degrees												
low	—41,2	—60,9	—65,8	—73,4	—75,7	—78,0	—80,7	—78,6	—76,6	—77,1	—54,8	—44,7
high	—21,5	—26,6	—47,8	—53,5	—49,7	—37,8	—52,7	—34,9	—39,5	—38,4	—33,4	—24,7
Mean air velocity, m/s	4,0	4,4	5,8	5,9	5,7	5,7	5,8	5,7	5,6	5,5	5,5	5,4
Maximum air vel., m/s	8,0	12,0	14,0	14,1	15,0	22,0	14,0	16,0	16,0	20,0	12,0	18,0
Mean relative humidity, %	75	71	70	69	70	71	70	72	71	70	70	70
Atmosph.press., mbar means:	637,5	631,0	630,0	627,2	624,8	631,2	622,5	631,4	623,8	617,8	622,1	632,1
minimum	627,4	616,2	615,0	617,2	614,4	614,8	607,4	614,4	604,8	604,6	614,6	621,8
maximum	648,2	649,8	646,6	641,6	634,2	642,4	644,6	652,8	640,1	638,2	632,4	641,4
Mean monthly temp. indoors, degrees	20,0	18,2	20,0	18,0	15,6	14,4	14,2	16,0	15,8	18,0	17,6	17,4

of mood, outbreaks of effective excitement, alternating with a feeling of repentance and depression. During the second stage of the expedition, the signs of the neurotic syndrome began to intensify and became distinct in many of the explorers. In the middle of the period of polar night, some individuals presented anxiety and depression symptoms. There was increased irritability, quick temper motivated by high volume of the tape recorder, etc.

The main manifestations of the astheno-neurotic syndrome were complaints of "helmet" type headache developing at the end of the work day, unstable mood, diminished libido and appearance of pollutions (hence anxious thoughts about impotence), itchy skin, diminished interest in the work, a need to frequently change activities and for longer sleep. In these individuals, sleep was restless, with fearful dreams, occasionally in color, with prevalence of reds and greens. Examination revealed vegetative disorders: diffuse pink or white dermographism, lasting up to 3-4 min, marked tremor of the fingers, eyelids, hyperhydrosis and a tendency toward constipation. There was also a tendency toward lowering of arterial pressure, mainly referable to systolic pressure. Drugs, psychotherapy and a few days' stay at the medical station improved their overall condition. With the advent of polar day, all of the individuals presented an emotional uplift; however, there was no visible improvement in their neuropsychological status.

Thus, development of a marked astheno-neurotic syndrome in most of the expedition members is indicative of significant tension of adaptation mechanisms of the organism. This is confirmed by the results of dynamic studies of their physical status. At the first stage of the expedition,

in spite of the high level of motor activity they displayed, both groups of individuals presented lowering of all parameters of their physical condition. At this stage of the expedition, appreciable hypodynamic changes could not yet have developed in the myoneural system, and this lowering should apparently be attributed to hypoxia of the organism, which had not adapted to this factor. Thereafter, the level of motor activity remained at about the same level in the 2d group of explorers, while the 1st group presented distinct signs of diminished physical qualitites: endurance related to force, postural dynamometry, static endurance of flexors of the trunk. There was no change in either group in static endurance of extensors of the trunk. Although the adaptational changes were less marked in the 2d group of expedition members, they did not undergo complete acclimatization.

There were signs of poorer supply of blood to the myocardium in individuals with the asthenoneurotic syndrome. Examination of higher nervous activity by the method of psychological observation revealed distinctive dynamics referable to the sociopsychological area. As in previous expeditions, we observed phases of becoming familiarized, discussion [or controversy] and orientation, which corresponded to a specific psychological tonus: even mood, restrained in the phase of familiarization, uplift, increased nervous excitability, talkativity, open encounters of the conflict type mainly expressed verbally (controversy phase), diminished affect, closed type of conflict tension, or in the case of open encounters, with a distinct vegetative-emotional component (orientation phase). Toward the middle of the expedition period, emotional orientation of the participants was completed and there was formation of stable, informal subgroups of 2-3 people in each. Conflict was observed not only between participants, but between subgroups. We must mention the difference in sociopsychological reactions of experienced explorers and those involved for the first time in such expeditions. The former were more stable, restrained, disciplined with little conflict, and they also presented less marked asthenoneurotic manifestations.

In view of the sensory "deprivation" at the station, particularly with regard to colors, selection of information media became very important: books, movies, etc. The explorers preferred documentaries and films with military and patriotic content, and especially in color. The decoration of living and working quarters acquired significance with regard to psychological status. Productivity of labor was diminished in the presence of monotony and uniformity of color, sparsity of elements made the participants unwilling to live in the same room for any length of time. All this prompted them to decorate their living and working quarters (paint the walls in different shades, esthetic execution of mess-halls, re-equipment of work places, raising plants, etc.), and this immediately resulted in elevation of general living tonus and efficiency.

The results of a set of biochemical and immunological tests broadened our knowledge about the neurohumoral mechanisms of adaptation of the human body to extreme conditions, particularly in the case of development of the astheno-neurotic syndrome (Tables 2 and 3). In the first month at the

station, the explorers presented increased excretion of catecholamines and 5-hydroxyindoleacetic acid (5-HIAA), and this was more marked in those participating in such an expedition for the first time. These data are indicative of some strain on the sympathoadrenal system, which could apparently be attributed to mobilization of compensatory mechanisms of adaptational dynamics of the organism in response to the deleterious living conditions and, first of all, to hypoxic hypoxia.

The recovery of most hormonal parameters toward the end of the 3d and beginning of the 4th month of the expedition could probably attributed to the fact that, by this time, adaptation to extreme conditions continued to occur by means of other compensatory mechanisms of the body. The new output of biologically active substances and elevation of other biochemical parameters (blood sugar, 11-HCS [hydroxycorticosteroids], serotonin) during the period of polar night are, in all probability, due to prolonged tension of regulatory systems due to appearance of a number of new stress factors inherent in polar night. These factors elicit certain metabolic changes and intensify catabolism of biologically active substances [6-8]. Elevation of levels of some biologically active substances in blood toward the end of the expedition can apparently be attributed to emotional excitement related to the news that the individuals would return to their homeland, as well as an increased volume of physical work.

By the end of the expeditionary period, the participants presented lower immunological resistance, in the form of lower levels of immunoglobulins and properdin in blood. The changes in nonspecific resistance of the organism were associated with a higher incidence of cases of colds, sore throat and neuromyositis.

The changes in peripheral blood reflected processes of adaptation of the organism to hypoxia, and they were manifested by elevation of hemoglobin level, increase in number of erythrocytes and thrombocytes, as well as redistribution of formed elements in the leukocyte formula.

Thus, the clinical and biochemical studies of individuals, who spent 1 year in Central Antarctica, confirmed the phasic nature of adaptation to extreme conditions with reference to the nervous and cardiovascular systems, and hormone metabolism. They were manifested in the form of general asthenization, neurotic reactions and changes in biogenous amines. These data confirm the fact that a 1 year stay in Central Antarctica elicits significant changes in various systems of the organism, which do not permit determination of adaptation to these conditions.

According to data referable to metabolism of biogenous amines, 11-hydroxycorticosteroids, sugar and certain other biochemical indices, in individuals with the asthenoneurotic syndrome the process of adaptation to deleterious conditions was protracted and, in some cases, did not occur at all.

Table 2. Excretion of biogenous amines (μg/day) and 5-HIAA (mg/day) in participants of the Vostok station during the 17th Soviet Antarctic expedition (M±m)

Index	Base level (before expedition)	Duration of mission, months				
		I	II	III	IV	V
Epinephrine:						
1st group	6,6±1,37	11,2±1,26			12,8±1,32	
2d "	8,6±0,63	10,7±1,72			10,3±1,2	
Norepinephrine:						
1st group	28,4±2,8	58,9±3,6			48,2±4,8	
2d "	25,9±3,2	39,4±4,4			27,8±3,8	
D [dopa]:						
1st group	57,5±6,8	69,1±12,4			62,4±8,4	
2d "	47,5±8,0	57,4±9,8			50,1±7,1	
DA [dopamine]:						
1st group	259,0±28,4	452,8±38,1			393,0±43,0	
2d "	239,0±31,3	337,0±36,0			220,0±28,0	
5-HIAA:						
1st group	6,44±0,44	11,4±0,64	8,8±0,48	6,8±0,64	7,0±0,56	7,4±0,42
2d "	6,24±0,56	7,40±0,36	7,10±0,42	6,60±0,38	6,22±0,40	6,80±0,46

	VI	VII	VIII	IX	X	XI	XII
Epinephrine:							
1st group			5,9±0,64	18,8±1,10			11,6±1,18
2d "			8,1±1,22	7,8±1,2			9,8±1,40
Norepinephrine:							
1st group			38,8±5,4	44,3±3,9			54,2±6,4
2d "			20,4±6,2	35,0±7,8			42,1±4,8

	VI	VII	VIII	IX	X	XI	XII
D:							
1st group			58,4±6,5	65,1±14,1			68,4±10,2
2d "			45,4±10,2	49,4±9,8			54,8±7,8
DA:							
1st group			242,0±32,4	320,0±41,4			368,0±41,4
2d "			236,0±28,6	264,0±32,8			289,0±34,6
5-HIAA:							
1st group	7,9±0,60	9,0±0,52	9,8±0,68	7,64±0,74	6,86±0,58	6,68±0,74	7,0±0,88
2d "	7,20±0,6	7,48±0,54	7,60±0,48	6,96±0,24	6,46±0,32	6,82±0,42	7,20±0,82

Table 3. Some biochemical and immunological indices of explorers at the Vostok station during the 17th Soviet Antarctic expedition (M±m)

Index	Base level	Duration of expedition, months				
		I	II	III	IV	V
Blood serotonin, μg/ml	0,045±0,01	0,062±0,01	0,035±0,015	0,038±0,01	0,032±0,01	0,054±0,02
11-HCS, μg%	13,2±1,08	17,6±5,2			14,4±3,4	16,5±2,8
Blood sugar, μg%	82,8±3,2	99,9±4,2	82,4±3,8	80,2±3,6	85,6±4,2	110,4±5,6
Properdin, units/ml	8,2±2,0				6,0±2,5	9,0±2,3
Immunoglobulins, mg/100 ml:						
A	230,8±30,0				201,9±25,4	237,3±25,2
I	1350,4±125,4				1245,5±108,4	1405,0±128,1
M	64,0±2,8				55,7±4,5	56,0±3,4

	VI	VII	VIII	IX	X	XI	XII
Blood serotonin, μg/ml	0,062±0,02	0,07±0,02	0,075±0,01	0,048±0,01	0,054±0,02	0,06±0,02	0,058±0,01
11-HCS, μg%	20,5±5,3		19,0±2,8	14,2±5,5			17,6±5,2
Blood sugar, μg%	92,4±4,2	88,6±3,4	98,4±8,2	82,6±6,8			96,4±6,2
Properdin, units/ml			13,0±2,6	6,0±2,2			1,0±0,3
Immunoglob., mg/100 ml:							
A			222,2±17,3	121,3±20,9			144,4±26,8
I			1333,0±52,4	852,0±89,5			438,4±70,5
M			60,0±2,4	38,7±4,0			36,9±2,9

At the first stage of the stay at the Vostok station, in the structure of overall morbidity there was prevalence of colds and trauma related to the large amount of physical labor out of doors; in the second and third stages, this applied to asthenoneurotic and pustular pathology. We observed exacerbation of undiagnosed pathology, which was protracted in nature and did not respond well to therapy. The prolonged period of living within a small group of people in total isolation and in a situation of constant danger permits fuller demonstration of the personality traits of individuals and their compatibility. The obtained data are very important to the screening of candidates for long space flights.

The intracontinental Vostok station can be used as a unique natural laboratory for the study of the combined effect on the human body of such extreme factors as isolation, hypoxia, monotony of environment and pace of life, prolonged restriction of motor activity, absence of changes in season, unusual lighting conditions, etc., which could be encountered in the same combination during long-term space flights.

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EFFECT OF PROLONGED HYPOKINESIA ON THE COURSE OF ACUTE ASEPTIC INFLAMMATION

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[Article by P. V. Vasil'yev, V. Ye. Belay, N. A. Gaydamakin, G. D. Glod, V. F. Lysak, Ye. P. Mel'nikova, S. V. Petrukhin and N. N. Uglova, submitted 5 Apr 76]

[Text] Some authors have voiced the opinion that the course of illness in space may differ appreciably in its expression, time of development and symptoms from the known "terrestrial" forms [1-3]. Such assumptions are not without grounds, since we know that the course of many pathological processes acquires new characteristics against the background of altered reactivity of the organism.

I. V. Konstantinova [9] established that hypokinesia induces signs of depression of specific immunological reactions in immunity organs (lymph nodes and spleen) of animals.

The works of M. I. Kozar' [10], G. P. Mikhaylovskiy et al. [11] showed that, during hypodynamia, there is depression of phagocytic activity of blood, lowering of properdin level, depletion of lysozyme activity of saliva and gastric juice, and diminished bactericidal function of the skin.

Kraus and Raab [12], Lawton [13] and others observed the onset of serious complications among individuals on strict bed rest, in the form of pneumonia, exacerbation of cholelithiasis and venous thrombosis.

G. P. Mikhaylovskiy et al. [11] observed rhinopharyngitis, catarrh of the upper respiratory tract and periodontitis in subjects participating in experiments involving 62-day hypokinesia.

Yet there are no data in the literature concerning the extent of the effects of prolonged restriction of movement on the course of a number of pathological processes, including inflammation. For this reason, our objective was to make an experimental study of the main distinctions in the course of aseptic inflammation.

Method

Studies were conducted on 390 albino rats initially weighing 150-200 g. We conducted three series of experiments: in the first, we investigated the effect of different periods (15, 28 and 60 days in the 1st to 3d groups, respectively) of hypokinesia on the course of inflammation; in the second series, we examined the effect of duration of readaptation (1, 3 and 7 days), and in the third series, the distinctions of development of an inflammatory process against the background of continued effect of restricted mobility. There were equivalent groups of control (intact) animals in each series.

Inflammation was produced by administration of 0.1 ml 3% formalin under the plantar aponeurosis of the hind limb under aseptic conditions. We assessed the dynamics of the inflammatory reaction according to local changes and some systemic changes. Oncometry was used to determine the severity of edema. In addition, we recorded the incidence of suppuration, as well as the time at which necrosis or a dry scab started to develop and when it ended. We measured skin temperature on the plantar surface of the inflamed and healthy limbs. We counted blood leukocytes, eosinophils and assayed fibrinogen. A total of 140 animals were submitted to pathomorphological examination in order to evaluate the focus of inflammation and changes in several organs and tissues.

Results and Discussion

Administration of a phlogogenic agent elicited the typical signs of inflammation inherent in the model of the pathological process chosen for our experiments, which has been described comprehensively by several authors [14-17].

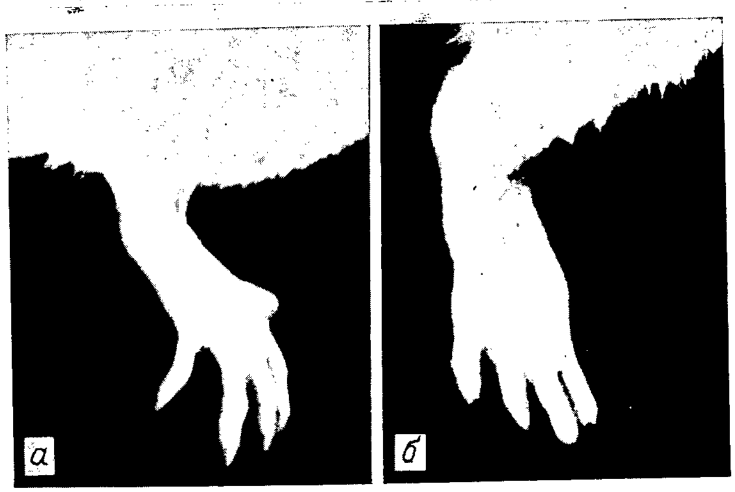

Figure 1. Development of inflammation in albino rat in response to administration of 0.1 ml 3% formalin solution

a) before giving formalin b) 4 h after the injection

Within a few min after administration of formalin, hyperemia of the foot appeared and edema developed (Figure 1), the latter reaching a maximum 6-24 h after the injection. When the course of inflammation was favorable, edema and temperature of the focus gradually diminished starting on the 3d-5th day, and by the 7th-10th day all outward signs of aseptic inflammation disappeared. In the case of development of complications, edema of the inflamed paw increased, involving the crus and thigh, with appearance of abscesses and necrotic foci. Complete resolution of the pathological process extended to the 30th-40th day and, as a rule, ended with formation of ankylosis of the ankle joints.

The above-described course of inflammatory reaction was typical in both control and experimental (hypokinetic) animals. However, the symptoms were more severe and complications were more frequent in experimental rats in all cases. For example, edema of the inflamed foot was 36.6-49.0% larger 4-24 h after giving formalin than in control animals, and there was a 1.1-1.4°C difference in temperature of the paws. We were impressed by the significant increase in edema, particularly after the 5th day of the inflammatory reaction. This was apparently due to secondary infection and development of complications (abscesses, necrosis). In experimental animals, the number of complications in the case of other terms of hypokinesia was always greater (see Table) and they were more severe.

Effect of hypokinesia on development of complications in the first series of experiments

Animal group	Rats/ group	Rats with necrosis:		P
		abs.	%	
Control	94	46	48,9±5,1	—
1	24	23	95,8±4,1	<0,01
2	30	22	73,3±8,1	<0,05
3	24	20	83,3±7,7	<0,05

We also observed substantial differences in size of edema and local temperature reaction in the second group of animals. Indeed, several experimental rats presented a significantly larger area of inflammation of the foot under the influence of the phlogogenic agent than the controls, while the difference in limb temperature constituted 2.5°C more than the control data.

Figure 2 illustrates the more general relationship between severity of edema and duration of hypokinesia.

On the basis of the results of pathomorphological studies, it can be noted that the changes in the inflammatory focus in animals submitted to hypokinesia were characterized by intensification of alterative processes, depressed formation of a demarcation zone, generalization of the process, slower resolution of necrotic masses and purification of the inflammatory focus,

as well as slower formation of granulation tissue. As an example, we can indicate that, as early as 1 day after administration of the phlogogenic agent, the experimental groups of rats presented edema of the corium, subcutaneous cellular tissue and underlying muscles, as well as a zone of vascular disorders involving considerably larger areas than in intact animals. In experimental rats, the leukocyte reaction was diffuse, extending in lingulate fashion over a considerable distance from the site of administration of the inflammation-inducing agent, and it did not form a distinct and continuous demarcation ridge circumscribing the necrotic region. The leukocytic ridge had fewer leukocytes, the vast majority of which were in a state of disintegration. There were fewer macrophages and lower phagocytic activity than in the control (Figure 3).

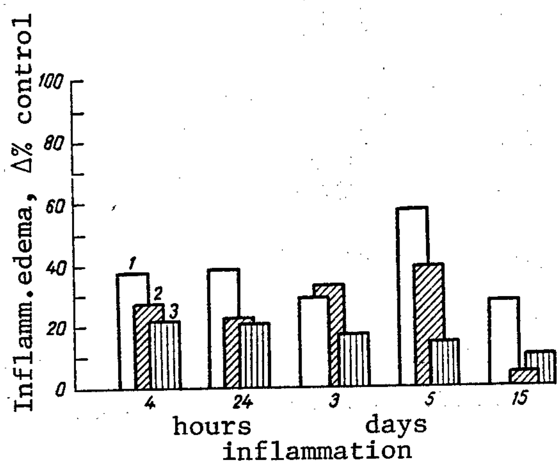

Figure 2.
Magnitude of inflammatory edema as function of duration of hypokinesia

1-3) hypokinesia for 15, 28 and 60 days, respectively

Against the background of continued restriction of motor activity, administration of the phlogoenic agent led to a decrease in external manifestations of the inflammatory process after 15 days: the differences in size of edema became statistically unreliable, and according to the changes in local temperature there was even a reliable decrease in the reaction, as compared to the control (4th h and 7th day of inflammation).

Readaptation time, during which the pathological process was induced, had some influence on severity of the inflammatory reaction. Thus, with administration of the phlogogenic agent on the 3d day of readaptation, the area of edema was somewhat smaller than when inflammation was induced on the 1st day after hypokinesia. The local temperature reaction was also less marked. In the case of inducing inflammation on the 7th day of readaptation, edema was, on the contrary, larger in some animals. The temperature change at the start of inflammation was greater than control data only in the 4th h; at other observation times, there were either insignificant differences, or even a statistically reliable less marked temperature reaction (7th and 15th days). Interestingly enough, the subsequent course of the pathological process was more favorable when the inflammatory agent was used on the 7th day of readaptation than at earlier times.

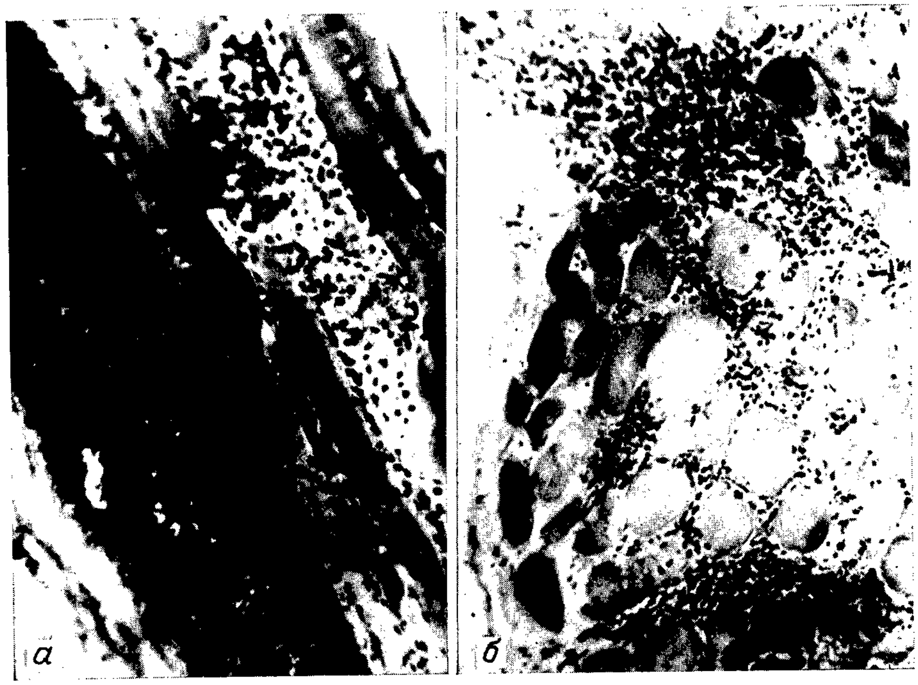

Figure 3. Formation of leukocytic ridge in control (a) and experimental (b) rats on the 1st day of inflammation after 15-day hypokinesia. Hematoxylin-eosin. Magnification 200×, objective 10.

Some distinctions were also noted, with reference to blood indices, morphology of tissues and organs, under the influence of the phlogogenic stimulus during or after hypokinesia. Thus, according to the hematological indices analyzed, inflammation after prolonged hypokinesia was associated with a distinctly attenuated neutrophil reaction, lack of phases in dynamics of total leukocyte content and greater eosinopenia, and all these changes were observed for a longer time in experimental rats.

The change in blood fibrinogen, which reflected the protective capabilities of the organism [18], was usually characterized by an appreciable decline after 15- and 28-day hypokinesia. Inflammation induced against this background was associated with elevation of blood fibrinogen. However, it is only after 15-day hypokinesia that there was a distinct and reliable decrease in the fibrinogen reaction to administration of the phlogogenic agent, as compared to control animals (Figure 4).

At other periods, the observed differences were statistically insignificant. Against the background of continued hypokinesia, administration of formalin elicited phasic changes in blood fibrinogen content in experimental animals.

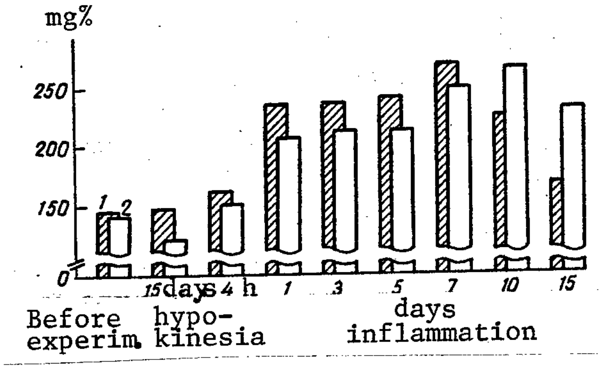

Figure 4.
Change in blood fibrinogen content in the presence of inflammation after 15-day hypokinesia

1) control
2) experiment

Readaptation for 7 days after hypokinesia led to restoration of blood fibrinogen level, and upon subsequent production of inflammation the fibrinogen content changes in experimental animals to about the same extent as in controls.

In almost all experimental series, there was a correlation between fibrinogen content and magnitude of edema and local temperature of the inflammatory focus. On the 7th-15th day, control animals presented a correlation between fibrinogen level and leukocyte content of blood, whereas in experimental animals, particularly in the case of inflammation against the background of continued hypokinesia, no correlation was observed between amount of fibrinogen and leukocyte content. Moreover, it was established that inflammation, in animals exposed to prolonged hypokinesia, was associated with more marked activation of morphofunctional state of the thyroid, severer changes in a number of structures of the central nervous system, as well as shifts in various directions (depending on duration of hypokinesia) with reference to adrenal reactions.

Thus, it was established that prolonged restriction of motor activity has a substantial effect on both the course of an inflammatory reaction and its outcome. It may be assumed that the course of a number of diseases characterized by acute inflammation (appendicitis, pneumonia, tonsillitis and others) would be more severe and require utmost caution with regard to prognosis of their development. No doubt, it will be necessary to develop special diagnostic methods and therapeutic principles. This opinion is backed up by the fact that complications are also observed in the course of a number of other pathological processes occurring against the background of hypokinesia which simulates, to some extent, the effects of weightlessness during long-term space flights [19].

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UDC: 615.916⁴126.2-31].015.45:612.12

EFFECTS OF CHRONIC EXPOSURE TO CARBON MONOXIDE ON BIOCHEMISTRY OF HUMAN BLOOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 46-50

[Article by M. V. Markaryan, T. A. Smirnova and O. S. Khokhlova, submitted 31 Jan 75]

[Text] Chronic carbon monoxide poisoning may be manifested by the most diverse symptoms and varying severity of changes in blood biochemistry [1-3]. However, investigations in this direction are sparse and contradictory.

In this work, we studied some aspects of protein carbohydrate and lipid metabolism in man as related to prolonged and continuous exposure to different concentrations of carbon monoxide. This is part of a set of joint studies pursued in order to set the maximum permissible concentrations of carbon monoxide in the atmosphere of pressurized [airtight] areas.

Methods

Four studies were conducted on 15 subjects ranging in age from 23 to 36 years, in a pressurized chamber 24 m^3 in size. The concentration of carbon monoxide in the atmosphere of the chamber constituted a mean of 20.3 mg/m^3 in the 1st study, 15.3 mg/m^3 in the 2d, 15.5 mg/m^3 in the 3d and 10.3 mg/m^3 in the 4th. Oxygen level was in the range of 19-22.4%, that of carbon dioxide, 0.42-0.67%; air temperature constituted 21-23.5° and humidity, 45-70%. The subjects were on a 2900 kcal diet, containing 147 g protein 113 g fat and 307 g carbohydrate. It consisted of canned meat and dairy products, first courses in cans and tubes, pastries, coffee and juices in tubes. The first 3 studies last 30 days each and the 4th, 90 days. Two 24-h emergency situations were created in the 3d and 4th experiments (on the 13th and 25th, and on the 20th and 32d days, respectively simulating malfunction of some life-support systems and aggravating living conditions.

We assayed total protein in blood serum by refractometry, protein fractions by means of electrophoresis, total lipids by the turbidimetric method [4], cholesterol according to Huang et al. [5], α- and β-lipoproteins by the method of electrophoresis on paper [6]. In the first three studies, we assayed fasting blood sugar by the anthrone method [7], and in the fourth,

we tested glucose tolerance after administration of 50 g sugar per os. We determined the level of glycemia on a fasting stomach, then 30, 60, 120, 150 and 180 min after sugar intake. The obtained data were submitted to statistical processing by the small sample method of Student.

Results and Discussion

As shown by the results of the 1st study, albumin level dropped from 5.49 to 4.65 g% on the 10th day of exposure to 20.3 mg/m carbon monoxide (Figure 1). Subsequently, though the albumin concentration did increase, it did not reach the base level. The β-globulin fraction underwent appreciable changes: it rose to 1.48 g% on the 28th day in all subjects, versus 1.00 g% at the start ($P<0.05$).

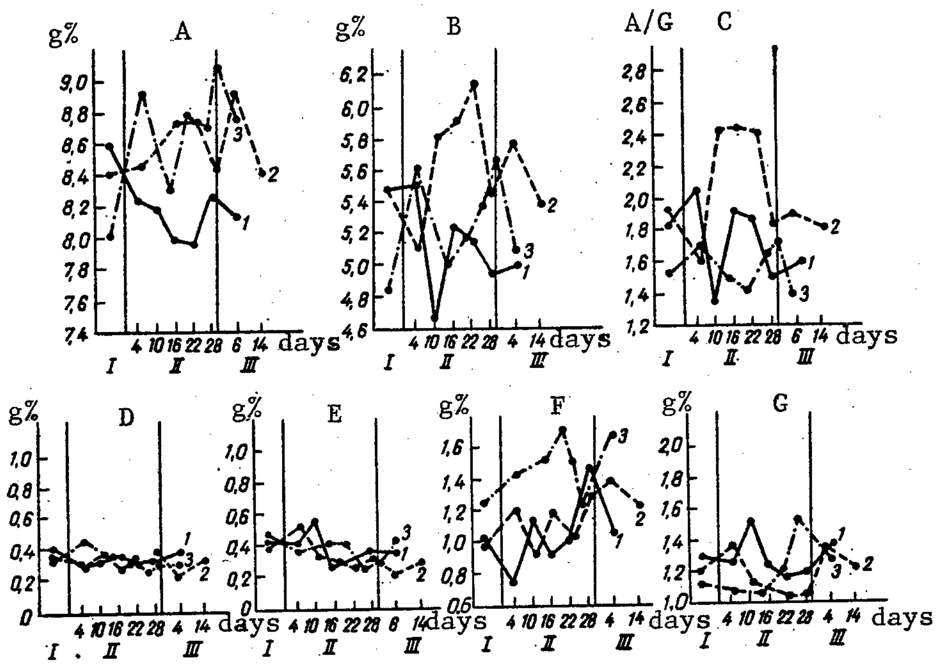

Figure 1. Blood serum proteins as related to carbon monoxide concentration in the pressurized chamber atmosphere.

A) total protein
B) albumins
C) corresponding albumin/globulin [A/G] ratio
D-G) α_1-, α_2-, β- and γ-globulins, respectively

Here an in Figures 2 and 3:
1-3) 1st, 2d and 3d studies (carbon monoxide content of 20.3, 15.3 and 15.5 mg/m^3, respectively)
I-III) initial, experimental and aftereffect periods

The experimental conditions elicited a drop of fasting blood sugar (Figure 2). On the 7th day, we observed a statistically reliable decrease in blood sugar from a mean of 107 to 68 mg% (individual range of fluctuations 66-70 mg%). Thereafter (12th, 18th and 24th days), the level of glycemia was appreciably lower than the base values and constituted 77, 75 and 78 mg%, respectively ($P<0.05$). By the 30th experimental day there was an increase in blood sugar (the difference was statistically reliable). On the 4th day of the after-effect period, we demonstrated an appreciable increase in glycemia in all subjects: blood sugar constituted a mean of 119 mg%.

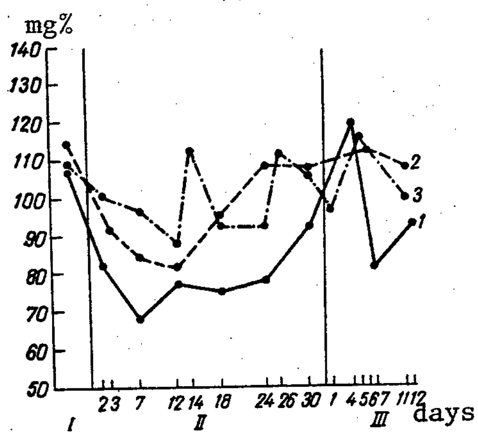

Figure 2.
Blood sugar level as function of concentration of carbon monoxide in the pressurized chamber atmosphere

The indices of lipid metabolism did not undergo significant changes (Figure 3), and we merely observed a tendency toward decline of total lipids and elevation of β-lipoproteins toward the end of the experimental period ($P>0.05$).

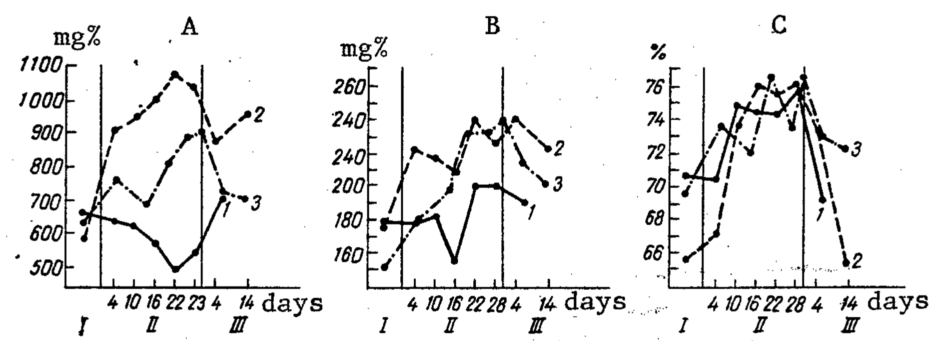

Figure 3. Dynamics of indices of lipid metabolism

A) total lipids B) cholesterol C) lipoproteins

In the second study, we observed an increase in blood serum albumin concentration by the 23d day of exposure. As compared to the base level, the difference

was reliable (6.14 g%, versus 5.49; $P<0.05$). By the end of the experimental period, the level of this fraction was close to the initial one. In this same study, there was a statistically reliable decline of glycemia, from 114 to 91 mg%, on the 3d day of exposure to an atmosphere containing 15.3 mg/m^3 carbon monoxide. There was also an appreciable decrease in blood sugar in 3 out of 4 subjects. On the 7th day, as was the case in the 1st study, we observed further decline of sugar concentration to a mean of 84 mg%. Sugar concentration held at this level up to the 12th experimental day ($P<0.01$). Tests made on the 18th day revealed some increase in glycemia, and blood sugar was close to the background level (108-107 mg%) only on the 24th and 30th days. On the 6th and 11th days of the aftereffect period, there was no appreciable difference in the subjects' blood sugar level, as compared to the indices obtained at the end of the experimental period (112 and 107 mg%, respectively). The indices of lipid metabolism rose appreciably: on the 4th day of exposure to carbon monoxide, total lipids increased from 587 to 908 mg% ($P<0.02$), and they were above normal on the 22d and 28th days: 1075 and 1-43 mg%, respectively. There was an increase in cholesterol content, but it did not exceed the physiological norm.

Indices of blood serum lipid metabolism in the subjects (4th study), M±m

Index	Base data	Experimental days			
		6	21	33	49
Total lipids, mg%	809±94	692±104	660±123	670±141	770±141
Cholesterol, mg%	192±50	205±32	182±36	185±29	210±27
β-Lipoproteins, %	74,0±0,9	78,3±1,3	73,5±3,8	78,1±1,4	79,6±1,9

Index	Experimental days				Aftereffect, 8th day
	64	71	84	90	
Total lipids, mg%	730±87	660±109	707±83	683±64	743±106
Cholesterol, mg%	206±36	189±30	204±49	203±31	185±33
β-Lipoproteins, %	82,2±0,9*	78,6±1,1*	75,7±1,4	76,1±2,3	74,2±3,1

* $P<0,05$.

In the 3d study, the proteinograms were indicative of a tendency toward increase in albumin concentration in the experimental period. The changes in the globulin fractions consisted of an increase in β- and γ-globulins. Thus, by the 20th experimental day, β-globulins constituted 1.72 g% ($P<0.01$). A second increase in level of this fraction was demonstrated on the 5th day of the aftereffect period (1.68 g%; $P<0.05$). A maximum increase in γ-globulins was demonstrated on the 26th day of exposure to carbon monoxide (1.53 g%; $P<0.05$). Along with an increase in these fractions, there was an increase in total protein concentration ($P<0.05$). In this study, we also observed a decreased level of glycemia and by the 12th experimental day blood sugar dropped from 107 to 88 mg% ($P>0.05$). In Figure 2, we are impressed by the

two increases in sugar concentration, on the 14th and 26th experimental days (to 112 and 111 mg%, respectively). The increased glycemia at these times coincided with the termination of "emergency situations," which could most likely be attributed to adrenalin hyperglycemia. Total lipid and cholesterol levels increased in the experimental period, as in the preceding experiments; the β-lipoprotein level rose in the experimental period. There was an appreciable decline of lipid metabolism indices in the aftereffect period.

In the fourth study, glucose tolerance tests failed to demonstrate disturbances referable to regulation of glycemia. No appreciable changes were demonstrated in total lipid and cholesterol levels as a result of 90-day exposure to carbon monoxide in a concentration of 10.3 mg/m^3. Their concentrations reached the base levels in the aftereffect period (see Table).

Thus, continuous 30-day exposure of man to carbon monoxide in a concentration of 20-15 mg/m^3 leads to impairment of metabolic processes, manifested by an increase in albumins and β-globulins, total lipids, cholesterol, β-lipoproteins and decrease in blood sugar concentration; 90-day exposure to an atmosphere containing 10 mg/m^3 carbon monoxide did not elicit appreciable changes in the parameters studied.

The submitted data confirm the fact that the biological effects of carbon monoxide exceed the range of hypoxemia due to hemoglobin blocking by this substance [1, 8, 12]. The demonstrated changes in the internal environment of the organism can apparently be attributed to the direct toxic effect of carbon monoxide on liver cells and enzyme systems involved in the metabolism of proteins, fats and carbohydrates [3, 13, 14]. As for the disturbances referable to carbohydrate metabolism, apparently increased utilization of glucose by brain tissues and other organs plays a rather important role in the mechanism of hypoglycemia [15].

The obtained data can be used to set maximum permissible concentrations of carbon monoxide in airtight areas.

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EFFECT OF SUPERHIGH INTENSITY CONSTANT MAGNETIC FIELDS ON MORPHOLOGICAL COMPOSITION OF PERIPHERAL BLOOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 50-55

[Article by A. G. Borodkina and Z. N. Nakhil'nitskaya, submitted 9 Oct 75]

[Text] Investigation of the correlation between the effect and intensity of the field is one of the approaches to demonstration of general patterns of the biological effect of magnetic fields. Most of the known works dealing with the biological effects of constant magnetic fields (CMF) were conducted with exposure to fields of up to 1000-5000 Oe. There have been only isolated studies using higher forces. In particular, we know of data pertaining to the reactions of the cardiovascular and respiratory systems to CMF of 62,500 to 70,000 Oe [1], the state of some hematological parameters under the influence of CMF of 8800 and 13,500 Oe [2] and changes in electrolyte excretion after exposure to 7200 and 14,000 Oe CMF. The present work deals with blood reactions to CMF in excess of 10,000 Oe with different exposure time.

Methods

Experiments were conducted using a superconducting electromagnet kindly provided by the Institute of Atomic Energy imeni I. V. Kurchatov. Experimental mice were exposed to horizontal CMF. The active zone had the shape of a cylinder 7.5 cm in diameter. The force of the CMF in the middle constituted 42.8 kOe, and it dropped to 5 kOe at the ends at a distance of 18 cm from both sides of the cylinder. There was no pulsation of CMF force. The experimental mice were placed in plexiglas boxes, with 5 animals in each, in the central region of the active zone (mean force of CMF, $H = 25.4$ kOe, $dH/dx = 3.5$ kOe/cm) and peripheral region of this zone ($H = 9.9$ kOe, $dH/dx = 1.6$ kOe/cm), and they were exposed to the CMF for 0.5, 1, 3, 8 and 24 h. One series of experiments was conducted in a more homogeneous field, with $H = 42\text{-}40$ kOe and exposure of 3 h. The mice were able to move freely within the box during exposure. They were provided with feed and fresh air by means of forced ventilation. The experimental animals were decapitated concurrently with controls at different intervals after removal from the box. We assayed hemoglobin level, erythrocytes,

reticulocytes and leukocytes, as well as the leukocyte formula in blood samples. Experiments were conducted on 380 CBA mice. There were 10 mice used at a time, 5 experimental and 5 controls.

Results and Discussion

The results of our studies revealed that exposure to CMF of 9.9, 25.4 and 39.4 kOe does not elicit changes in total number of erythrocytes or hemoglobin level in them, either immediately after exposure or in the next 35 days. However, we did demonstrate changes in blood reticulocyte content. The direction of the changes depended on duration of exposure and time that had elapsed after it. Signs of reticulocytosis were observed during 24-h exposure to CMF of 39.4 kOe after the first 30-min. With increase in exposure time to 1.3 and 8 h, the number of reticulocytes dropped to the level in the control or lower, whereas reticulocytosis was again demonstrated after 24-h exposure. Figure 1A illustrates data pertaining to reticulocyte content of blood in the course of 24-h exposure of mice. The readings were made immediately after removing the animals from the magnetic field. As can be see in Figure 1, reticulocyte content constituted 163±37% of the control after 30-min exposure; 90±26, 86±14 and 83±34% after exposure for 1, 3 and 8 h, respectively, and rose to 163±44% after 24-h exposure.

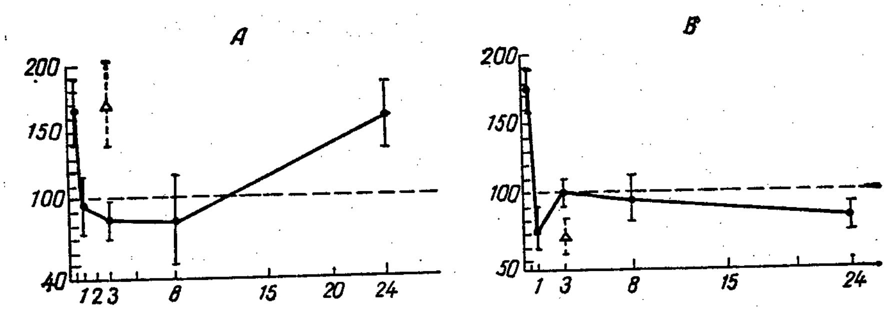

Figure 1. Reticulocyte content (A) and leukocytes (B) of peripheral blood in the course of 24-h exposure to CMF of 39.4 kOe. X-axis, exposure time (h); y-axis, cell content (% of control)

With exposure to a relatively homogeneous CMF, H = 40-42 kOe, the signs of reticulocytosis persisted for a longer time than in a heterogeneous field for 3 h of exposure (Figure 1, vertical dotted line), whereas in a heterogeneous field the number of reticulocytes decreased at this time.

The changes in reticulocyte content observed immediately after exposure persisted in the early aftereffect period and presented the same direction. One day after 30-min exposure the number of reticulocytes (as was the case immediately after exposure) was reliably increased and constituted 144±20% of the corresponding control. No reliable differences in reticulocyte content in experimental and control groups of animals were demonstrated 1 day after 1- and 3-h exposure.

Investigation of the effects of a homogeneous field 1 day after 3-h exposure revealed, as was the case immediately after exposure, that the reticulocyte content remained high, constituting 146±13% of the corresponding control.

In evaluating erythrocyte reactions at the longer term after exposure, we found some dynamics to reticulocyte content in peripheral blood of mice. The nature of the reaction was unrelated to the force of the field. In the case of 3-h exposure in CMF of 39.4, 25.4 and 9.9 kOe, after an initial decrease in reticulocytes, which was observed immediately after exposure, there was a transient increase on the 2d day, which was subsequently followed by another decrease. Throughout the observation period (up to 20 days, and 35 days in 2 series), the reticulocyte content remained lower than in the control, although the decline was not always statistically reliable (Figure 2). As can be seen in Figure 2A, the increase in number of reticulocytes, as compared to the base level, on the 1st-2d day was unreliable; however, it was obvious, as compared to the amount of reticulocytes preceding the increase. A wave of elevation was observed consistently in all cases and, like its magnitude, it was unrelated to the force of the magnetic field. The increase in reticulocytes in the case of 3-h exposure did not exceed 35%. At the same time, the initial decrease in reticulocyte content was the most marked with the lowest force, H = 9.9 kOe and it diminished with increase in field force.

Some changes were demonstrated in blood leukocytes. Figure 2B illustrates data on dynamics of leukocyte content in the course of 24-h exposure to CMF with H = 39.4 kOe. Figure 2B shows that signs of leukocytosis (175% of the corresponding control) observed after 30 min of exposure are replaced by leukopenia (70% of base level) when exposure extends to 1 h. With increase in exposure time to 3 and 8 h, there is normalization of this index, and after 24-h exposure we again observe signs of leukopenia (80% of base level).

With exposure of animals to more homogeneous CMF, H = 40-42 kOe, the initial leukopenia persisted for a longer time than in a heterogeneous field. It was still demonstrable after 3-h exposure (see Figure 1B, vertical dotted line), when leukocyte content constituted 65% of the corresponding control. At this time, normalization of leukocyte content was observed in a heterogeneous field. A study of the dynamics of total leukocyte content for the first 24 h after 30-min, 1- and 3-h exposure to CMF, H = 39.4 kOe, also revealed undulant changes. Within 20 h after termination of exposure to CMF, with all of the parameters tested, there was a decrease in number of leukocytes. Their number increased somewhat in the blood of experimental animals 24 h after exposure. It constituted 125±21% of the corresponding control in the case of 30-min exposure, 137±23% with 1-h exposure and 123±34% with 3-h exposure. The leukocyte formula of these animals indicated that the leukopenia observed in the first few hours after exposure develops as a result of decrease in number of both neutrophils and lymphocytes. The increase in leukocytes toward the end of the first 24 h was due to normalization of lymphocyte content and significant increase in number of neutrophils.

Figure 2B illustrates the dynamics of leukocyte content after 3-h exposure to CMF of different force. As we see, immediately after exposure to CMF,

H = 25.4 Oe and 9.9 kOe, there was an increase in total number of leukocytes to 70 and 65% of the base level. Thereafter, on the 1st-2d day, leukocyte content rose. After exposure to CMF of 25.4 kOe, it reached 139±21% and after 9.9 kOe, 130±11.7%. At the same time, with the highest of the used CMF forces (39.4 Oe), we failed to observe an initial phase of decrease in leukocyte content, while only a tendency toward increasing was noted on the 2d day. At this time, blood leukocyte content was 9% higher than the base level, and this was not statistically reliable. At the longer postexposure terms, with all field forces used, we observed a decrease in leukocyte content. With the lowest force (H = 9.9 kOe), this was demonstrable at the later stages, 10 days after exposure, whereas with H = 39.4 and 25.4 kOe it was observed on the 3d-5th postexposure day. There was a more significant decline with the smaller field forces of H = 9.9 and 25.4 kOe. By the 20th day, the leukocyte content constituted 68±9.5% and 68±8.8%, respectively, of the base level. With a force of 39.4 kOe, it constituted 85±13.1%. A study of the leukocyte formula during the aftereffect period revealed that the decrease in leukocyte content was due to a decline in number of both neutrophils and lymphocytes, i.e., the lymphocyte profile of blood inherent in mice was retained.

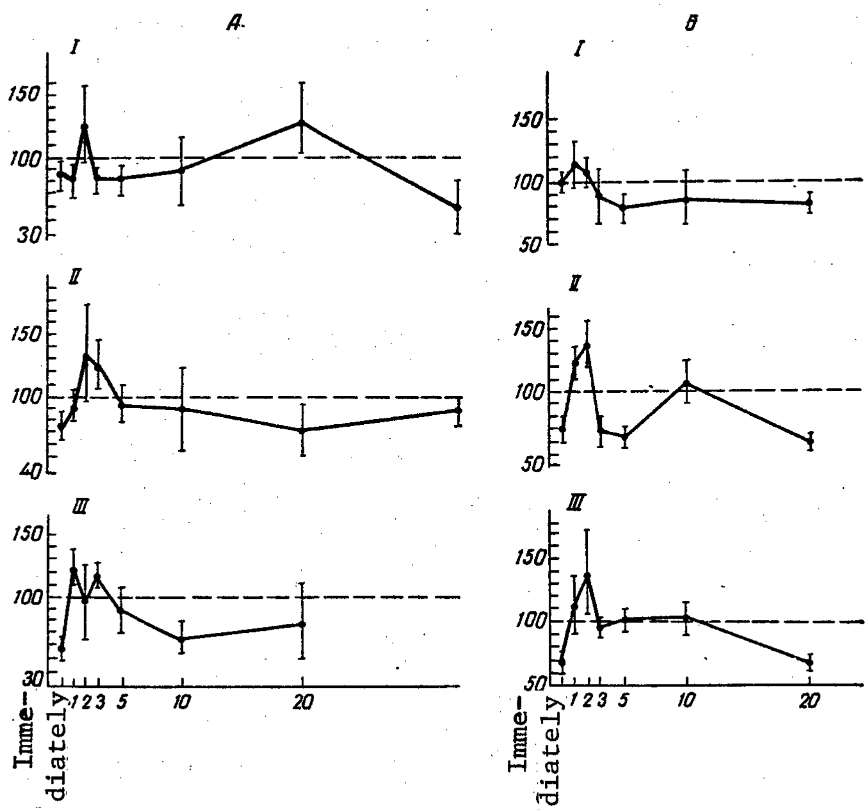

Figure 2. Reticulocyte (A) and leukocyte (B) content of peripheral blood after 3-h exposure to CMF varying in force. Y-axis, cell content (% of control); x-axis, postexposure time of examination (days). Force: I) 39.4 kOe•g•1.1 kOe/cm II) 25.4 kOe•g•3.5 kOe/cm III) 9.9 kOe•g•1.6 kOe/cm

Thus, exposure of mice to CMF of 9.9, 25.4 and 39.4 kOe elicits changes in reticulocyte and leukocyte content of peripheral blood. During 1-h exposure to CMF of 39.4 kOe, as well as in the aftereffect period following 3-h exposure, using all of the above-mentioned forces, these changes are phasic: periods of increased reticulocyte and leukocyte levels alternate with periods of decreased levels. The general direction of changes during the first 8 h of exposure to CMF of 39.4 kOe in number of reticulocytes, leukocytes, neutrophils and lymphocytes favors the assumption that blood is redistributed. By the end of 24-h exposure, differences are demonstrable in reactions of white and red blood. The changes in reticulocyte and leukocyte content persist for a long time in the aftereffect period, for over 20 days. We were impressed by the consistent elevation of these indices on the 1st-2d postexposure days. The changes in reticulocyte and leukocyte content were not excessive; they were unrelated to the force of the field within the tested range. The number of reticulocytes increased to the same extent as with exposure to a considerably lower intensity, i.e., 1000 Oe. Some increase in extent of decline of reticulocyte and leukocyte content with increase in field force, observed immediately after exposure, is most likely attributable to faster development of the reaction with high field forces, as a result of which the tendency toward recovery and subsequent increase is demonstrable sooner.

We had also observed signs of reticulocytosis previously using CMF of lower intensity, 1000 Oe or less. This effect has also been observed by other investigators. For the time being, the genesis of reticulocytosis is not known. While the early increase in reticulocyte, as well as leukocyte, content is related to a redistributional reaction, the reticulocytosis that develops later is most likely indicative of intensified erythropoiesis. There are grounds to relate this reaction of the erythroid system to development of tissular hypoxia under the influence of CMF. Although onset of the latter requires experimental confirmation, it appears to be quite plausible, due to the demonstrated changes, under the influence of CMF, in oxygen-binding properties of hemoglobin and, as a result of this, impaired tissular oxygenation.

Unlike the erythroid reaction to low-intensity CMF, at 10 kOe or more, after a brief increase we observed a persistent and prolonged decrease in number of reticulocytes with concurrent decrease in leukocytes, which is apparently related to depression of erythropoiesis and leukopoiesis.

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UDC: 612.273.2.014.482.4

ORGANISM REACTIONS TO HYPOXIA FOLLOWING EXPOSURE TO GAMMA RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1977 pp 55-59

[Article by B. I. Davydov and V. V. Antipov, submitted 2 Dec 75]

[Text] Investigation of reactivity of an organism exposed to ionizing radiation to the effect of acute hypoxia is of interest to aviation and space medicine. There is no agreement in the literature as to how the irradiated organism reacts to acute hypoxia. Most authors [1-4] report increased resistance to hypoxia in irradiated animals; others [5, 6] report that it decreases. It is difficult to compare all these data, since the studies were mostly conducted without consideration of dose and, particularly, time parameters.

As we did in our research with G forces [7, 8], we tried to make a quantitative evaluation of endurance of single exposure to hypoxia of the irradiated organism, as related to radiation dosage and time of development of the radiation effect.

Methods

Experiments were conducted on 620 mongrel mice and 248 rats. The animals were exposed to gamma rays in doses of 200-4000 R at the rate of 50 R/min. The animals were put in a pressure chamber 2-20 days after irradiation. The "climb" rate constituted 20 m/s. The animals were kept at an altitude of 10 km (mice) and 12 km (rats) until all of them expired.

The correlation between time of exposure to hypoxia and mortality can be described as a cumulative function ["cumulate"] (performance curve). For this reason, one can use the method of probit analysis to calculate both the mean effective time (ET_{50}) of animal death and animal death in the case of a fixed time of exposure to hypoxia. In addition, we calculated the median (Me) time. In the latter case, radiation death without hypoxia was evaluated as zero time. The arithmetic mean time was determined only for mice that died within 30-min exposure to hypoxia.

Results and Discussion

Preliminary studies revealed that within the early postradiation period (2-4 h), using doses of 850-2000 R, there is an increase in mouse resistance to acute hypoxia by about 0.5 km [9].

Table 1. Mouse resistance to acute hypoxia (H = 10 km) during the period of acute radiation sickness (20 animals in each irradiated group, 120 in the control)

Postradiation time, days	Dose, R	Me,min ($P=0,05$)	$\bar{x}\pm\sigma_{\bar{x}}$, min**	ET_{50}, min*
Control	0	2,7 (1,9÷5,6)	3,2±0,9	2,6
2	200	3,9 (3,9÷6,0)	4,7±0,8	3,7
	300	5,7 (3,7÷15,0)	4,7±1,6	5,3
	500	4,5 (3,2÷5,7)	4,2±0,8	3,7
	800	2,3 (1,5÷30)	2,2±0,7	2,7
	2000	2,5 (2,0÷30)	2,4±0,8	2,3
4	200	10,0 (3,0÷30)	3,5±1,3	5,1
	300	4,9 (3,3÷7,7)	2,8±0,5	4,5
	500	2,5 (2,0÷4,5)	2,8±0,5	4,5
	800	2,3 (1,0÷3,3)	2,0±0,5	2,0
10	200	4,4 (2,7÷6,5)	4,3±0,9	3,2
	300	3,8 (2,2÷5,5)	4,0±1,2	3,4
	500	3,0 (2,0÷4,6)	3,3±0,1	3,0
	800	1,4 (1,0÷2,5)	2,9±1,0	1,5
15	200	11,0 (3,1÷30)	5,1±3,2	5,4
	300	6,6 (5,3÷30)	7,3±2,6	6,6
	500	6,1 (1,5÷30)	4,2±1,9	5,6
	800	2,0 (1,0÷5,3)	3,6±1,5	2,1
20	200	4,1 (3,5÷5,6)	5,1±1,4	4,0
	300	4,0 (2,5÷4,7)	4,0±1,1	3,9
	500	2,5 (2,0÷4,3)	3,2±1,0	2,8
	800	0,9 (0÷4,1)	4,7±0,8	0,5
30	200	2,7 (1,5÷5,8)	3,5±1,0	2,8
	300	3,2 (2,5÷4,9)	3,8±0,9	3,1
	500	2,7 (1,0÷5,0)	4,3±1,7	2,7
	800	1,7 (0÷2,2)	2,6±0,7	1,3

*Counting deaths prior to irradiation.
**Hypoxia, 30 min

We observed a constant tendency toward increased resistance to hypoxia with doses of 200-500 R, virtually throughout the observation period (Tables 1 and 2). With doses of 800-2000 R, there was a change in endurance of hypoxia, in the direction of worsening, on the 2d postradiation day. Greater variability of the animals' reaction to hypoxia was inherent in irradiated animals, as compared to controls. In the experiments with rats, the dosage of gamma radiation was selected each time so as to obtain interpolated doses of radiation, at which endurance of hypoxia was the same as in the control.

Resistance of irradiated mice and rats to hypoxia depends on the radiation dosage and time of development of radiation sickness. With regard to the

time parameters, these changes are similar to the reactions of irradiated animals to G forces [10-13]. As a rule, the values of radiation doses were obtained by interpolation, and they elicited virtually no change in sensitivity to hypoxia. The obtained values are illustrated in Figure 1 as a dose-time function.

Table 2. Resistance of irradiated rats to acute hypoxia (H = 12 km) (8 animals per group)

Postradiation time, days	Dose, R	$\bar{x}\pm\sigma_x$, min	Me, min
1	0	10,2±4,7	6,5
	600	19,1±5,1	18,2
	800	23,8±4,9	27,8
	2000	15,3±3,3	14,9
	4000	10,5±4,2	11,6
2	0	12,0±5,7	10,7
	600	17,8±5,3	18,5
	800	22,6±5,2	29,9
	1000	24,8±4,8	20,5
	2000	13,7±5,3	12,3
5	0	17,0±4,3	17,5
	200	19,2±3,8	18,4
	400	16,6±4,7	16,5
	800	13,7±4,1	10,0
7	0	16,6±5,5	14,4
	200	17,9±2,8	16,0
	400	16,6±2,7	20,5
	600	12,9±2,8	12,4
	800	10,6±3,8	9,2
10	0	15,9±2,9	12,0
	200	22,3±5,8	29,7
	400	11,1±3,6	11,9
	600	10,0±2,2	8,1
15	0	12,2±2,1	11,4
	100	15,8±2,8	12,2
	200	13,6±3,7	14,9
	400	10,3±6,7	12,9
20	0	9,7±2,3	8,4
	100	20,4±6,8	20,9
	200	15,9±4,5	17,1
	400	13,9±0,9	15,1

Previously [7], we found that the dosage and time after radiation, at which endurance of G forces did not differ from that of control animals, are related to the "mean life expectancy--dose" curve, but in the case of irradiation alone. This correlation is more marked in evaluating dose tolerance as function of time of development of the radiation effect, according to the criterion of resistance to acute hypoxia (see Figure 1).

A comparison of the curves of "spontaneous" radiation and "forced" death due to hypoxia leads us to the following conclusions: In the first place, the decrease in resistance to hypoxia of irradiated animals appears to precede radiation death (far beyond the range of the confidence interval, P = 0.05; curve 5); in the second place, curve 1-2 can be approximated to

a hyperbole, $Dt = 3 \cdot 10^3$ ($1<t<20$), where D is the dose of gamma radiation, R; t is postradiation time (days). The coefficient of this equation is about 50% smaller than with G forces, and this is apparently indicative of the "harsher" effect of hypoxia than the former. Evidently, with a milder effect of hypoxia, curve 1-2 will approximate the curve of "natural" radiation death. Finally, we can assume that there is a family of curves of endurance of hypoxia as related to partial oxygen pressure. The critical PO_2 level, at which endurance of irradiated and healthy animals will be the same, is 10-12 mm Hg at an altitude of 15.5 km [14]. This is the altitude at which the time of onset of paralysis of vital centers does not alter appreciably, according to the data in [15].

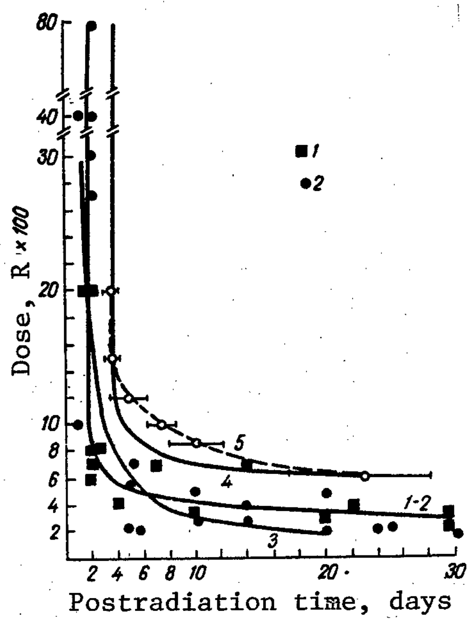

Figure 1.
Resistance of irradiated animals to acute hypoxia as function of dose and time
1) mice
2) rats
3) hyperbolic approximation
4) mean life expectance of irradiated animals according to B. Rayevskiy
5) the same, according to our data

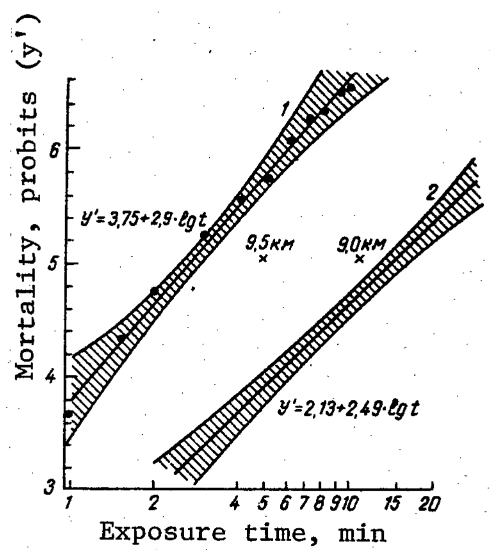

Figure 2.
Mouse deaths due to acute hypoxic hypoxia at 10 km altitude (1) and transverse G forces of 44 units (2) as function of time of exposure.

The x's refer to mean effective time of death at 9.5 and 9.0 km altitudes

A comparison of the results of studies obtained with exposure of the organism to G forces and acute hypoxia impresses us with the existence of some similarity of changes (Figure 2). It is remarkable that common changes, inherent in the effects of these two factors, are also demonstrable on the EEG [11]. Furthermore, as stressed by O. G. Gazenko et al. [6], it is harder to demonstrate differences that are specific to each factor than similarities.

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CATARACTOGENIC EFFECT OF 25 and 50 MeV PROTONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 59-62

[Article by A. N. Kabachenko and B. S. Fedorenko, submitted 30 Oct 75]

[Text] It is known that protons of different energies constitute the main component of cosmic radiation. In the course of long-term space flights, one cannot rule out their effect on spacecraft crews, and this diminishes the efficiency of cosmonauts. As reported previously [1, 2], in the case of a solar burst, the radiation dose to superficial layers of tissues, including the eyes, could be higher by a factor of 10^1 or 10^2 (depending on protection factors, etc.) than to deep tissues, since low and moderate energy protons constitute the main part of solar radiation. In this regard, there is reason to believe that these particles could present a real danger to the eyes of cosmonauts, particularly the lens.

In the few works [306] dealing with the effects of protons on the lens of experimental animals, it was shown that 20-100 MeV protons have a cataractogenic action.

Our objective was to investigate the incidence of radiation cataract in mice and time of appearance thereof under the influence of 25 and 50 MeV protons, as well as 200 kV x-radiation.

Methods

In our experiments, we used male $CBA \times C_{57}Bl_6$ mice weighing 16-18 g. The animals were exposed to a single dose of local radiation (head region) using 25 and 50 MeV protons (dose rate of 0.4 rad/s) and 200 kV x-rays (dose rate 5 R/s, 15 mA, 0.5 mm Cu + 1 mm Al filters) in doses of 100, 200, 400 and 600 rad. A nonirradiated group of animals served as the control.

We checked the lens of irradiated and control animals every 2 weeks using an electroophthalmoscope and +15.0 D magnifying glass. The pupils were dilated with 1% homatropine. We used a method, which classifies opacities into four stages [7] and was proposed for small laboratory animals, to evaluate lenticular opacities. The incidence of such opacities was estimated on the basis of the ratio of eyes with opacities to total number of eyes in each group of animals, and it was recorded as a percentage.

Results and Discussion

The results of our investigation revealed that opacity of the lens occurred in mice exposed to 25 and 50 MeV protons, as well as x-rays in doses of 100-600 rad, the clinical development of which was analogous to that observed with exposure to other forms of ionizing radiation [8, 9]. There was a difference in time of manifestation of lenticular opacities, depending on the dosage, i.e., a difference in latency period, which diminished with increase in dosage. Thus, with exposure to protons and x-rays in doses of 400 and 600 rad, the first opacities were recorded 10 weeks after exposure; in the case of doses of 100 and 200 rad, they appeared after 15 weeks. Analysis revealed that the duration of the latency period of formation of a specific level of opacities as function of dosage is analogous to the function we previously described for 645 MeV protons [10]. This function is linear. Processing of the results obtained by the least squares method failed to demonstrate differences between the effects of 25 and 50 MeV protons and 200 kV x-rays.

The incidence of opacities in irradiated animals increased with increase in dosage (Table 1). The incidence of opacities as function of dosage can also be described by a linear equation in the dose range of 100-600 rad:

$$N = \beta D + c,$$

where N is the incidence of opacities (%); D is dosage (rad); c is the incidence of opacities in control animals (%) and β is the coefficient of proportionality of a straight line, corresponding in this instance to the change in incidence of opacities with 1-rad change in dosage. The values of coefficient β are listed in Table 2.

Table 1. Incidence of lenticular opacities in mice exposed to 25 and 50 MeV protons and 200 kV x-rays at different postexposure times (M±m)

Postradiation time, weeks	Radiation dose, rad	Incidence of opacities, %			
		exposure to			control
		protons		x-rays	
		25 MeV	50 MeV		
	100	1,2±0,16	1,4±0,15	1,1±0,19	
15	200	1,9±0,13	2,6±1,80	1,8±0,25	—
	400	6,9±2,47	5,0±2,23	6,4±2,45	
	600	8,3±2,81	11,3±3,20	12,4±4,48	
	100	19,3±4,20	16,3±5,22	23,3±4,80	
	200	18,2±3,74	11,0±3,28	37,3±4,65	5,7±2,27
30	400	44,1±1,73	44,7±4,95	63,6±5,25	
	600	45,8±5,08	45,7±5,38	87,0±1,40	
	100	47,5±5,51	45,3±2,64	58,4±2,44	
40	200	58,0±1,64	60,0±5,15	78,6±4,00	13,2±3,31
	400	82,3±5,29	80,0±4,54	100,0	
	600	85,7±3,64	85,9±4,64	100,0	

Table 2. Changes in coefficient β as function of examination time (M±m)

Postradiation time, weeks	Exposure to protons 25 MeV	50 MeV	x-rays	P
15	0,01±0,001	0,02±0,001	0,02±0,002	⩾0,5
30	0,07±0,005	0,07±0,005	0,13±0,010	⩽0,01
40	0,15±0,020	0,15±0,020	0,23±0,050	⩽0,05
55	0,16±0,010	0,16±0,010	0,20±0,030	⩽0,01

Note: P is the criterion of reliability of differences between effects of 25 and 50 MeV protons and x-rays.

It is apparent from the submitted data that the intensity of lenticular opacities is the same under the influence of 25 and 50 MeV protons, and that it increases up to a certain time (in this instance, up to 40 weeks). The value of coefficient β does not change thereafter. We also see that β is higher for x-rays than protons, which is indicative of the fact that the latter are somewhat less effective.

The lower effectiveness of moderate energy protons, as compared to x-rays, is probably attributable to differences in dose rate. As we know from the literature [11, 12], an increase in radiation dose rate leads to a more marked radiation effect. Since we were unable to make a study of the cataractogenic effect of protons of moderate energy and x-rays at the same dose rate, we tried to make experimental determination of the adjustment for dose rate. For this purpose, we made a special study of the effect of dose rate of 645 MeV protons on incidence of opacities in mice. The results of this investigation revealed that an increase in dose rate by a factor of 10 leads to a 1.9±0.2-fold increase in incidence of lenticular opacities. In comparing the biological effects of 25 and 50 MeV protons and x-rays, we took this fact into consideration and made a correction in estimates of coefficients of relative biological effectiveness (RBE) of protons of the tested energies. The RBE coefficients of protons according to the criterion of incidence of opacities were calculated by comparing the doses of standard proton radiation leading to opacities in 50% of the cases to formation of opacities within a specific time after irradiation. The RBE coefficients for 25 and 50 MeV protons were found to be similar (0.9±0.1) at all tested times.

Investigation of the dynamics of development of opacities in mice exposed to protons also revealed that the incidence thereof is related to time that elapses after exposure (see Table 1). This is also a linear function and the coefficient of proportionality constitutes 1.0-1.4 and 1.6-1.8 for doses of 100 and 200 rad, 1.8-2.5 and 2.0-2.8 for doses of 400 and 600 rad protons and x-rays, respectively. As we see, the values of the coefficient of proportionality increase with increase in dosage of protons and x-rays.

Development of the different stages of lenticular opacities in mice exposed to 25 and 50 MeV protons occurred less intensively, unlike the animals exposed

to x-rays. In the former case, mainly grade I and II opacities developed and it is only 30-35 weeks after exposure to protons in a dosage of 600 rad that we observed grade III opacities in 1-2% of the cases. At this time, grade III opacities constituted 35% in mice exposed to 600 rad x-rays. The demonstrated differences in effects of protons and x-rays on incidence and intensity of development of radiation cataracts in mice were quantitative, and, as noted before, they were due to the lower dose rate of protons.

Thus, this investigation established that 25 and 50 MeV protons have definite cataractogenic activity. The incidence of lenticular opacities occurring under the influence of protons is a function of dosage and postradiation time. A comparison of equally effective doses of protons and x-rays, with regard to cataractogenic activity, revealed that the RBE of 25 and 50 MeV protons is close to 1. The linear nature of incidence of opacities as function of dose and postradiation time is indicative of absence of correlation between proton RBE coefficients and examination time and dose levels used as a criterion of vulnerability to radiation. A study of the distinctions of formation of different grades [stages] of opacities revealed consistent development of radiation cataract under the influence of protons and x-rays. This is indicative of the lack of any specific manifestations of cataractogenic action of protons. Consequently, one can apparently be guided by the relevant data obtained from studies of the effects of standard forms of radiation in resolving problems of protection, prognosis and therapy of radiation lesions to the lens.

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ACUTE LEUKOCYTIC REACTIONS TO IMPACT ACCELERATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1977 pp 62-67

[Article by Ye. Ye. Simonov, submitted 19 Feb 75]

[Text] Estimation of leukocytes in blood is a mandatory element of comprehensive clinicophysiological and laboratory examination of individuals exposed to impact accelerations. The results of this type of studies play a substantial role in arriving at expert conclusions and sometimes determine the nature thereof. Any more or less appreciable deviation from the base level serves as grounds for excluding subjects from participating in experiments and, on the contrary, the absence of changes is interpreted as an argument in favor of continuing with experiments.

In our opinion, there are insufficient grounds for such an approach to evaluation of the significance of changes in number of leukocytes circulating in blood when the organism is exposed to impact accelerations, since we know that it is not every type of acute leukocytic reaction that can be considered pathological [1, 2, 5, 8].

According to current conceptions, acute leukocytic reactions, manifested by an increase in number of leukocytes and observed with exposure to very many factors, including some that are not deleterious, are in essence a normal physiological response of the organism reflecting its capacity for adaptation and mobilization [5]. As a rule, leukocytic reactions of this type occur under the influence of stimuli that do not elicit supraliminal inhibition in the central nervous system (CNS) or a "breakdown" of effector mechanisms responsible for the leukocytic reaction. However, excessively strong stimuli can induce changes in typical reactions, with regard to both their magnitude and direction. One observes accentuated leukocytic reactions, attenuate (no increase in leukocytes) or "paradoxical" reactions, i.e., a decrease instead of increase in number of leukocytes [5, 8].

This circumstance suggests that only a distorted type of leukocyte reaction, constituting the result of impairment of mechanisms of regulation of leukocyte level in blood, could serve as a reliable index of the pathological influence of the agent under study on the organism. Apparently, it is

expressly from these positions that one should also approach evaluation of changes in leukocyte content of blood under the influence of impact accelerations on man and animals.

Our study of variants of acute leukocyte reactions of animals, exposed to impact accelerations of increasing intensity, ranging from a level known to be nondeleterious to those eliciting a distinct traumatic effect, was made in order to verify the foregoing.

The need for experimentation over a wide range of intensities of this factor rules out the possibility of making such tests with the participation of humans. Of course, this diminishes, to some extent, the value of the data obtained. Nevertheless, this circumstance does not preclude subsequent extrapolation of the results of our studies, since the general patterns of reactions of the system under study are basically the same in man and animals.

Methods

Experiments were conducted on male albino rats weighing 200-300 g, divided into 9 groups of 6 rats each. The first two groups of animals were not exposed to impact accelerations and served to study the leukocyte changes occurring in response to stimuli related to transportation to the site of the experiments, immobilization, etc. The rats in the other groups (3d-9th) were exposed to the impact accelerations encountered during landings reproduced in an SUP-10 stand [4, 6]. The magnitude of back--chest accelerations was determined by calculations [6]. These groups of animals served as a model for the study of leukocyte reactions developing as a result of the combined effect of nonspecific (transportation, immobilization) and specific (impact accelerations) stimuli.

In the control experiments and those with impact accelerations, pairs of animals were placed belly down on the surface of the dropping platform of the stand and they were immobilized by means of soft bands on the legs. They remained immobilized for no more than 5-10 min.

We assessed the intensity of the effect of accelerations according to both the animals' general condition and behavior, and nature of lesions to internal organs demonstrated at autopsy. We used rats sacrificed immediately after exposure (4-6 in each experiment) for pathomorphological analysis. We used ether fumes to sacrifice the animals.

The Table lists the characteristics of experimental physical parameters and biological effects induced by the experimental factors.

We took blood for tests from the tip of the tail on the eve of the experiments (background) then 4 h, 1, 2, 3 and 5 days after. Using the blender method, we assayed the total leukocyte count and eosinophils per mm^3 blood, and the leukocyte formula in smears stained according to Romanovskiy. We calculated the absolute number of different forms of leukocytes from the results of counting total leukocytes and percentile levels of different forms. The obtained data were submitted to statistical analysis.

Experimental conditions and biological effects of landing-related accelerations

Experiment groups	Parameters: landing rate, m/s	Parameters: G forces, units	Biological effects: animal behavior and general condition	Biological effects: macroscopic changes in internal organs
1 (control)	Transportation to experimental site and back		No distinctions	None
2 (control)	Same + immobilization on stand platform + elevation and gradual lowering of platform			
3	3	400—600		
4	7,5	(345—410)×3*	Increased motor activity, aggressiveness. No deaths.	Fine focal extravasations into lungs, and in isolated instances into the liver.
5	7,5	550—610		
6	10	485—505		
7	7,5	(500—600)×3*	Paresis of hind legs, adynamia, higher threshold for sonic and other stimuli. Deaths	Extravasations into soft tissues of anterior thoracic and abdominal walls, focal extravasations into abdominal organs, multiple focal and total extravasations into the lungs and under epicardium
8	7,5	(500—600)×3*		
9	10	730—780		

Note: Asterisks refer to number of exposures at 3-5-min intervals.

Results and Discussion

As can be seen in the Table, we failed to demonstrate any changes whatsoever in behavior and general condition after the tests in animals of the 1st-3d groups. They presented no pathomorphological changes referable to internal organs and, in particular, upon microscopic examination of tissues. This warrants the conclusion that the stimuli involved in these cases, including specific ones, i.e., impact accelerations of 400-600 units at a landing rate of 3 m/s, did not elicit a deleterious (pathological) effect. Consequently, the 1st-3d groups of animals can be considered a combined "active" control, suitable for the study of nonspecific (stress) reactions of the organism.

The Table indicates that the 4th-6th groups of rats were exposed to impact accelerations in the range of 345-610 units and a landing rate of 7.5-10 m/s. Under these conditions, the animals presented an increase in motor activity and aggressiveness. Autopsies revealed pinpoint extravasations of blood, localized primarily in the lungs. In this case, the stimuli could be qualified as tolerable but inducing a primary traumatic effect (this conclusion is completely consistent with the data of other researchers [4]).

The animals in the 7th-9th groups were exposed to impact accelerations of 500-780 units at a landing rate of 7.5-10 m/s. These factors elicited more marked signs of trauma (adynamia, paresis of the hind limbs, etc.), as well as pathomorphological changes in tissues and organs. In this case, extravasations were demonstrable not only in lung tissue, but in abdominal organs, soft tissues of the thoracic and abdominal walls. Some animals presented effusions under the epicardium with lethal outcome. We qualified such stimuli as intolerable.

Thus, in essence we were dealing with three categories of stimuli: 1) relatively mild (1st-3d groups of rats) that did not induce visible changes in tonus of the CNS; 2) moderate (4th-6th groups of animals) leading to distinct excitation of the CNS; 3) excessive (7th-9th groups) eliciting development of excitatory processes in the CNS following exposure.

According to existing conceptions [4, 8], one should have expected that the animals in the 1st-3d groups would either develop no leukocytic reactions, or else they would be of the moderate, hyperleukocytic type. In the 4th-6th groups of rats, we could have expected demonstration of distinct hyperleukocytosis, whereas in the 7th-9th groups there could have been leukocyte dynamics of any type inherent to states associated with impairment of mechanisms of regulation of leukocyte level in blood. The obtained data confirm the validity of these hypotheses. Thus, the 1st-3d groups of animals presented some increase in leukocyte level in blood (statistically unreliable) with a maximum 1 day after the experiment. Investigation of the "leukocyte profile" according to Mashkovskiy revealed that, in the 1st group of animals, hyperleukocytosis was due to the concurrent increase in number of lymphocytes (bulk of "white" cells circulating in rat blood) and neutrophils. In the 2d and 3d groups of rats, against the background of elevation of neutrophil content observed 4 h after the experiment, there was a minor decrease in absolute number of lymphocytes. Later on, 1-3 days later, the number of lymphocytes also increased and was above the base level. It must be indicated that, in all instances, the increase in number of neutrophil leukocytes was associated with an increase in both stab and segmented forms, with a concurrent sharp decrease in eosinophils, particularly in the first (after 4 h) blood test.

The leukocytic reactions of rats in the 4th-6th groups differed little from those described above. Here, as in the preceding experiments, there was development of hyperleukocytosis, with increase in number of stab and segmented neutrophils. At first (after 4 h) there was a decrease in number of lymphocytes, whereas it exceeded the base level later on. There was a

concurrent decrease in number of eosinophils. However, a maximum extent of changes in total leukocyte content in these cases was observed 2 days after the experiments, rather than the 1st postexperimental day. Thus, the total duration of the period of primary increase in number of leukocytes was somewhat longer in the 4th-6th groups of rats. Thereafter, the leukocyte level declined, but did not reach the base level. It must be stressed that, in these experiments, the degree of maximum increase in total number of leukocytes was greater than in the preceding experiments. In other words, while the changes in total number of leukocytes and different forms thereof in animals of comparable groups (1st-3d and 4th-6th) were virtually the same with regard to quality, they differed somewhat in quantity: there was a more marked increase in number of leukocytes circulating in blood under the influence of stronger stimuli. On this basis, it may be concluded that, over a specific range of intensities of stimuli, acute leukocyte reactions are governed by the law of regular force relations, which establishes proportionality between the magnitude of the response and force of the stimulus.

The nature of the leukocytic reactions differed appreciably under the influence of intolerable accelerations (7th-9th groups), as compared to the experiments discussed. Immediately after exposure, the number of leukocytes increased only in one test and showed virtually no change in the two others. Thereafter, there was a more or less appreciable decrease in their number, which remained below the base level almost to the end of the observation period.

Analysis of the curves referable to number of different types of leukocytes revealed that, against the background of demonstrated changes in total number of leukocytes in the first few hours, the neutrophil content increased; later on there was a tendency toward decrease, so that the the curve of neutrophil number as a whole repeated the curve of total leukocyte content. At all tested times, the lymphocyte level was below the base value. There was a decrease in number of eosinophils after 4 h; thereafter it increased and exceeded base levels.

The obtained data indicate that, in each of the cases discussed, the blood leukocyte level does not remain unchanged in experimental animals. A moderate increase in leukocytes is observed under the influence of mild stimuli, related to transportation, immobilization of the animals and even the effect of nondeleterious landing-related accelerations, and this is apparently due to relatively minor excitation of the CNS and subsequent changes in neurohumoral status. Hyperleukocytosis of this type could be equated with the reflex leukocytic reactions observed in the presence of emotional [3] and physical [7, 10] tension, overheating [9] and other types of stress states. The leukocytic reactions induced by accelerations that elicit a primary deleterious effect are apparently of analogous origin. However, in this instance, the presence of microtraumatic changes is an additional stimulus for reaction on the part of systems of emergency elevation of blood leukocyte level, which leads to a longer increase in number of leukocytes. The same direction and qualitative resemblance of changes in the experiments involving nondeleterious and minimally deleterious

stimuli do not justify qualification of this type of leukocytic reaction as being pathological. According to all of the data, such reactions are a special manifestation of the organism's general defense reaction, a unique gauge of the physiological response to the stimulus. Only the changes observed in experiments with intolerable accelerations could be classified as the pathological type of acute leukocytic reaction. The results of these experiments revealed that, in this case, we were dealing with distorted leukocyte reactions with subsequent decrease in total number of leukocytes. Such acute leukocytic reactions indicates that, under these specific conditions, the organism was no longer capable of normal reactions to the stimulus and that its different adaptational mechanisms, including "emergency" increase in blood leukocytes, were profoundly damaged.

The foregoing is indicative of a need to revise conventional conceptions of the diagnostic value of changes in total number of leukocytes circulating in blood with exposure to impact accelerations.

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INVESTIGATION OF PERSONALITY TRAITS OF PILOTS AND NAVIGATORS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 67-70

[Article by N. F. Luk'yanova, V. I. Polyanskiy and Ye. N. Lokshina, submitted 24 Feb 75]

[Text] The question of upgrading psychological screening of flight personnel continues to be one of the most important problems of aerospace medicine. Up to the present time, in psychological screening for aviation, only one psychological aspect is taken into consideration in our country: the quality of mental processes (perception, thinking, memory, sensorimotor qualities, attention and a few others), while distinctions referable to temperament and character are not investigated enough.

Yet these personality traits are among the factors that determine achievement in flight activities.

Investigation of personality traits that assure optimum performance of flight missions is one of the means of further improvement of psychological screening of flight personnel. It would be impossible to solve this problem without formation of an "ideal" of personality traits of pilots and navigators which, as we know, is the final stage of professiographic studies [1].

Methods

There has not been adequate development of a methodological approach to the study of pilot personality. Diverse methods are used for this purpose: observation, conversation, various questionnaires and scales. After testing several methods, we are now using a specially selected set of techniques.

SMIL is an adapted variant of the Minnesota Multiphasic Personality Inventory (MMPI). The method consists of 550 statements dealing with general physical condition, cardiovascular, gastrointestinal, neurological and other disorders, family and sexual relations, habits, general social and ethical sets, self-evaluation, etc.

The 16-factor personality questionnaire makes it possible to gain an idea about the personality distinctions referable to such polar factors as restraint--gregariousness, concrete thinking--abstract thinking, initiative--performance, trust--suspicion, emotionality--reasonability, flexibility--persistence, group dependence--independence, conservatism--innovativeness, fearfulness--decisiveness and others. In addition, secondary factors are derived: extraversion, independence, reactive equilibirium, anxiety [3, 5, 9].

The distinctions of motivation were studied using a variant of the thematic apperception test (TAT) developed by Heckhausen [8, 11]. This modification of the well-known projective test examines motivation and the desire to reach a goal. In addition to the intensity of striving for a goal, it demonstrates the correlation between activity of two motivations: the hope for success and fear of failure. The prevalence of one of these motivations or equilibrium thereof permits obtaining the qualitative and quantitative characteristics of motivation. The test consists of a set of six pictures of the situational type, which are exhibited to the subject in turn. Special pictures are selected for the test, where the situations meet two main requirements. With rather distinct and vivid representation of the "cast" and objects, the very composition of these situations is also objectively vague, so that no unequivocal interpretation is possible. When perceiving such pictures, the subject has the illusion of an absolutely clear picture: definite images immediately define the area of action of the subject, his environment and directions of reaction but, at the same time, the vagueness of the composition (which rules out unequivocal and identical answers) compels the testee to interpret the picture in his own way. The subject gives his own values to each interpretation. In other words, his answers, so to speak, project his personality traits on a "screen."

The myokinetic psychodiagnostic test is based on the thesis that the motor system is not only an external expression of mental activity, but an important component of formation and integration of mental functions. The author of the test, Mira-y-Lopez [2, 6], adheres to the principle of myokinetic dissociation, according to which the motor activity of the dominant half of the body (right in right-handed individuals) depends more on the prevailing characterological reactions, whereas motor activity of the subdominant half of the body (left in right-handed individuals) is more related to manifestations of temperament, i.e., the congenital distinctions of an individual. The principle involved in the test is related to performance of specific movements in the main planes of space (horizontal, vertical and sagittal) without visual monitoring. Graphic production is evaluated. As a result of processing the results of the test, quantitative indices are obtained of the degree of manifestation of different personality traits, reflected in motor activity, such as psychomotor tonus, anxiety as a personality trait, level of anxiety prevailing at the time, emotionality, extraversion and introversion.

This set of methods was used to test 137 pilots and 34 navigators ranging in age from 25 to 33 years, with tenure of 5 to 10 years.

Results and Discussion

Figures 1 and 2 illustrate averaged personality profiles obtained from testing both groups by the SMIL method and 16-factor personality questionnaire. The data obtained from the SMIL test are within the normal range in the pilots and navigators examined (from 30 to 70 in T norms) as established by the authors of the original [10] and adapted [7] variants. Analysis of the obtained results enabled us to single out several main personality traits common to all tested individuals.

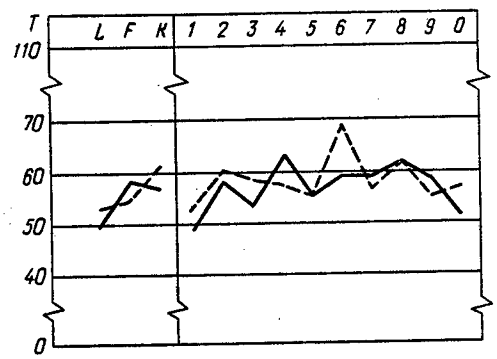

Figure 1. Averaged results of SMIL test on groups of pilots (solid line) and navigators (dotted line)

Brief description of SMIL scale:

L, F, K) scales for determination of reliability of test performance
1) degree of concern of testee with his health
2) tendency toward worrying, control of emotions
3) emotional lability, social flexibility, conformity
4) tendency to take changes, impulsiveness, high level of pretensions
5) masculine and feminine traits, direction of sexual interests
6) rigidity of judgments, "harshness" of sets, persistence, perseverance
7) anxiety, psychasthenic traits
8) originality of thinking and perception, intuitiveness
9) level of activity and optimism
0) social introversion--extraversion

All of them are energetic, active, they have initiative, purposefulness, and a highly developed sense of duty and responsibility. They are characterized by the ability to defend their opinion; they are capable and are not afraid of taking chances, and they act rationally under stress conditions. They hold an effective position in solving vital problems and have a rather high level of motivations to reach their goal, and self-confidence. At the same time, there are several personality traits inherent to representatives of each of the groups individually.

Thus, pilots present more vivid emotionality, greater desire for leadership, high self-evaluation and level of pretensions. This is indicated by the

elevations on scales 4, 8 and 9, with low curves on scales 1 and 3 (see Figure 1). They present a higher level of social activity (high curve on scale 9 and low on 0). In addition, pilots present a somewhat elevated anxiety level (scale 7 of the SMIL and elevation of factor 0 on the 16-factor personality questionnaire)(see Figure 2). Some degree of this property is needed in the structure of a balanced personality, since it determines a well-developed sense of responsibility, ability to anticipate hazards, rapid orientation with unexpected changes in a situation. Moreover, the elevation on scale 7 presents a positive correlation with such a personality trait as a high degree of responsibility.

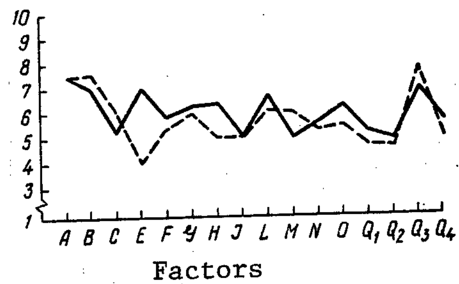

Figure 2. Averaged data pertaining to 16-factor personality questionnaire on groups of pilots (solid line) and navigators (dotted line)

Brief description of factors:

A) restraint--gregariousness
B) concrete thinking--abstract thinking
C) sensitivity--stability, rationality
E) flexibility--dominance
F) seriousness--joy of living
G) initiative--performance
H) lack of confidence--decisiveness
I) emotional maturity,--realistic--tendency toward fantasizing, refinement
L) trustfulness, adaptability--lack of flexibility, preference of one's own opinion
M) practicality--impracticality
N) lack of sophistication [ingenuousness]--calculation
0) self-confidence--anxiety
Q_1) conservatism--innovative
Q_2) group dependence--independence
Q_3) inner conflict--self-control
Q_4) attenuated calmness--high motivation

Some increase in anxiety, observed in the tested group of pilots, should be distinguished from a high degree of anxiety as a constant personality trait, which could cause disorganization of actions under extreme conditions, loss of self-confidence, increased concern about health and diminish the effectiveness of performance of occupational operations. Interestingly enough, the somewhat elevated anxiety level in pilots is compensated by a

index of striving for a goal (according to TAT results), and there is prevalence of self-confidence in the structure of motivation. Analysis of the results of myokinetic psychodiagnostics revealed deliberate self-control in the group of pilots and this, along with self-confidence, is a good compensatory mechanism for the somewhat increased emotionality. Some elevations on scales 2, 5 and 7 of the SMIL test is also indicative of control of emotions.

With respect to analysis of personality traits of navigators, we were impressed by the statistically reliable elevation, as compared to the pilot group, on scale 6 of SMIL. This means that navigators are characterized by greater emotional stability than pilots. A certain rigidity of thinking, with a tendency toward formation of stable sets, the desire to systematize data and some pedantism are inherent in them. At the same time, they are more conformist (scale 3 of SMIL is higher than scale 4, and factor Q_3 is elevated in the 16-factor personality questionnaire); they always try to conform their actions to the decisions of the group leader. The index of drive toward a goal is somewhat lower in navigators than pilots, although confidence of success also prevails in motivation.

In view of the foregoing, it may be assumed that achievement of high results in the professional activities of pilots and navigators is related, along with many other conditions, to personality distinctions and correct choice of flying as a specialty.

Thus, the use of this set of methods of examining the personality yields information that sheds comprehensive light on various aspects of the personality, with reciprocal enhancement of reliability of criteria, and it permits quantitative evaluation of test results.

The above data have a direct bearing on improvement of occupational psychological screening for flying schools. In our opinion, examination of personality traits of candidates will make it possible to evaluate more fully, and this means more accurately, the fitness for flight training and provides a more substantiated individual approach to the educational and training process, as well as psychological training of flight personnel.

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TETRAPOLAR RHEOGRAPHY USED TO EVALUATE THE CIRCULATORY SYSTEM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 70-74

[Article by I. B. Tikhomirov (deceased), V. F. Turchaninova, V. T. Selivanenko and V. A. Staferov, submitted 5 Apr 76]

[Text] There is no information in the Soviet literature on the use of tetrapolar rheography.

In this work, tetrapolar rheography was used to determine pulsed delivery of blood to a given area; we tested the possibility of using this technique for quantitative description of cardiac output and blood flow in an extremity.

Methods

We used a tetrapolar rheograph developed for special conditions. Its characteristics are: 120 kHz for the working frequency of the generator, 2 mA measuring current, 0.3-70 Hz transmission band, 20 to 210 Ω range of possible measurements of resistance. We examined 65 individuals in all: 15 essentially healthy people (volunteers) ranging in age from 18 to 36 years and 50 patients with congenital disease of the heart and great vessels. We made 300 measurements of cardiac output. Blood flow in the limbs was determined (250 times) in patients with pathology of the vessels of the upper and lower extremities, coarctation of the aorta and other congenital heart disease (before and after surgery).

The clinical use of tetrapolar rheography was preceded by synchronous determination (on volunteers) of cardiac output by the dye dilution method, and with the tetrapolar rheograph and 4RG-1A rheographic attachment. The studies were conducted under metabolic conditions. We recorded the rheogram of the trunk to estimate cardiac output by the method of A. A. Kedrov. We used circular lead electrodes, 10-12 mm wide, to record the rheograms. The operating principle of tetrapolar rheography requires four electrodes for recording the rheograms in one lead, two of which are for the generator and two are removable. The removable electrodes must be between the generator ones. When taking rheograms of the trunk, the removable electrodes were placed on the boundary between the upper and middle thirds of both arms, and the

generator ones in the distal parts of the upper and lower limbs. This placement of electrodes yielded a longitudinal rheogram of the region under study under identical conditions for dynamic observations. We used a Mingograph-61 for recording, with paper feeding rate of 25 mm/s.

The trunk rheogram was recorded during a shallow, calm expiration, and those of the arms and legs, with the subject breathing calmly. Before starting the tracing, we determined interelectrode resistance. The rheograph made it possible to measure both total resistance, consisting of electrode--skin resistances and that of the examined region, as well as tissular resistance alone. Upon completion of the tracing, we recorded a calibration signal which constituted 0.1 Ω. Calculation of cardiac output and relative pulsed delivery of blood to the limbs using the following formulas:

$$\Delta V = \frac{\Delta R}{R} \cdot P \; ; \quad \Delta V_1 = \frac{\Delta R_1}{R_1} \cdot P_1$$

$$\Delta R = \frac{H}{h} \cdot 0{,}1 \; \Omega,$$

where ΔV is stroke volume (ml); ΔV_1 is relative pulsed delivery of blood to the limbs (ml/100 g tissue); P is weight (in g or cm); P_1 is 100 g tissue; R and R_1 refer to resistance of the examined segment of tissue (in Ω); H is amplitude of the rheogram (mm) and *h* is magnitude of the calibration signal (mm).

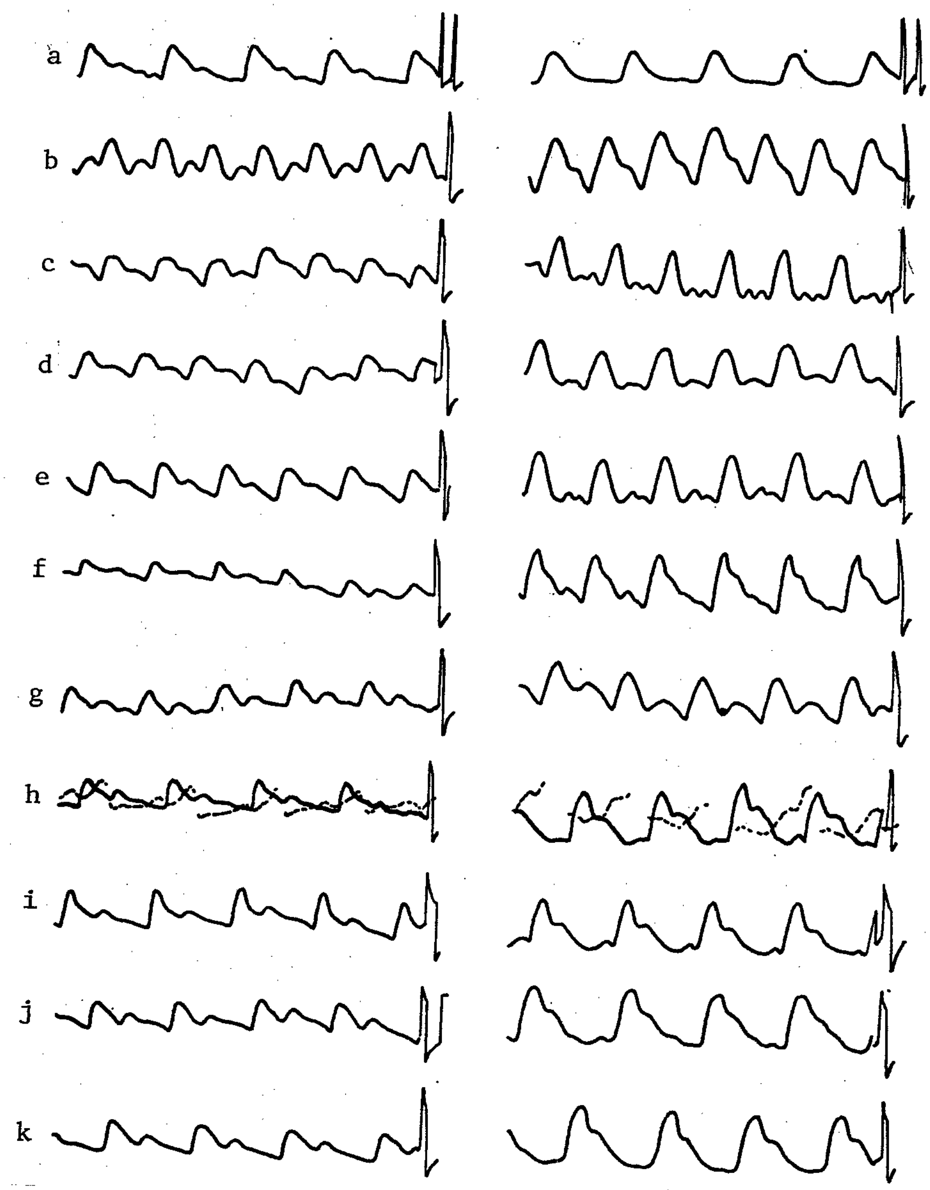
In the calculations, we used the averaged amplitude of several rheographic complexes. The minute volume of circulation, in liters, and magnitude of relative pulsed delivery of blood to the limb (in ml/min/100 g tissue) were determined by multiplying ΔV and ΔV_1 by the heart rate.

When using the dye dilution method, we adhered to conditions specified for tests using the tracer method [1]. We used Evans blue as the dye. The dye was given at the rate of no more than 0.15mg/kg body weight. We used a type 0-36M oxyhemograph to record the dye dilution curves, with a photoelectric ear-type sensor made of a silicon photoelectric cell. Some refinements were made to improve the accuracy of oxyhemograph readings: we increased tape-feeding speed to 160 mm/min, developed a new amplifer that was 8 times more sensitive and stabilized the power source.

Results and Discussion

The cardiac output, as determined by the dye dilution method, ranged from 4.0 to 9.36 *l*/min (6.24±1.56). The results obtained with the use of the tetrapolar rheograph differed little from control data and ranged from 3.1 to 9.4 *l*/min (6.0±1.64). The coefficient of correlation between these values is 0.96. Use of the 4RG-1A rheographic attachment yielded substantially

different results, as compared to the control. In this case, cardiac output ranged from 5.8 to 12.4 l/min. The coefficient of correlation between figures obtained by the control method and with the 4RG-1A rheographic attachment is 0.08.



Rheograms of the arm (on the left) and leg (on the right)

a) background
b) 5 h later
c) 1st day, morning
d) 1st day, evening
e-k) 2d, 3d, 5th, 10th, 15th, 18th and 21st days, respectively

Thereafter, the studies were conducted using only the tetrapolar rheograph. Comparative determination of cardiac output of patients before surgery by means of tetrapolar rheography and dye dilution revealed that there was no more than a 6% difference between the results. According to the rheographic data, the early postoperative period is associated with diminished cardiac output (in patients with coarctation of the aorta examined by both methods at the same time), while the dye-dilution method was indicative of an increase; as a result there was a 21.4% difference between the compared levels. At later postoperative stages (4th-10th days) both methods showed unidirectional changes in cardiac output, and the difference between them did not exceed 14%.

Pulsed delivery of blood to the arm constituted 2.25 ml/min/100 g tissue in the healthy arm and only 0.5 ml/min/100 g tissue in the involved arm in patients with occlusion of the brachial artery. Determination of circulation in the arm also revealed a decrease in the involved arm: 1.13 versus 1.89 ml/min/100 g tissue in the healthy arm. Analogous results were obtained on patients with occlusion of the femoral artery. Blood supply to the healthy leg was better than to the involved one, constituting 2.0 and 1.5 ml/min/100 g tissue, respectively. In patients with coarctation of the aorta, preoperative circulation in the arm, which was 3.38 ml/min/100 g tissue, was better than in the leg (2.31 ml/min). The individual differences in blood supply to the arms were in the range of 1.94-4.5 ml/min/100 g tissue and to the leg, 0.99-2.5 ml/min. After surgery, the correlations changed: there was a significant increase in relative pulsed delivery of blood to the lower limbs and it constituted 3.3 to 5.96 ml/min/100 g tissue in different patients. Dynamic observation of relative quantitative characteristics of pulsed delivery of blood to the limbs at different stages of the postoperative period was informative. Disturbances referable to functional state of the vascular wall were associated with quantitative changes in blood supply.

Analysis of the shapes of the curves revealed that the rheogram recorded on the tetrapolar rheograph presented all the typical signs: anacrotic notch, catacrotic notch with dicrotic wave. On rheograms of the limbs, we encountered additional notches, which were more marked on rheograms of the arms. In the postoperative period, a decrease or increase of vascular tonus was reflected by the shape of the rheographic tracing, mainly its catacrotic slope, and they were manifested by the dynamics of level and accentuation of dicrotic and additional notches (see Figure).

The rheographic method is based on the existence of a close link between cardiac function and pulsed fluctuations of tissular resistance. The results obtained are indicative of the feasibility of using tetrapolar rheography for this purpose; it permits not only qualitative, but quantitative evaluation of pulsed delivery of blood to the region examined. A comparison of cardiac output obtained by rheography and the dye dilution method revealed a high degree of correlation. Analogous results were also obtained by other authors [2]. The advantage of tetrapolar rheography is that the current through the generator electrodes is stabilized by the high input resistance of the

generator, while the measuring electrodes are connected to a circuit with high input resistance, so that the electrode--skin resistance does not affect the accuracy of the measurements. When using other types of rheographs, the bridge one in particular, a change in degree of contact between the electrodes and skin and shifting of the electrodes can alter the electrode-skin resistance to a degree that is considerably greater than the changes in resistance of the tissue examined. By virtue of stabilization of measuring current, the tetrapolar method permits obtaining comparable results from diverse experiments.

However, determination of cardiac output on the basis of resistance of the tissue region studied alone requires addition of a "correction" coefficient to the calculation formula, and this coefficient constitutes 0.73. We used the following formula for our calculations.

$$\Delta V = \frac{\Delta R}{R} \cdot P \cdot 0.73.$$

The design of the instrument permitted measurement of resistance with an accuracy of 5 Ω. The high stability of the instrument made frequent calibrations unnecessary, and this facilitated the examinations.

This type of rheograph was used to obtain cardiac output levels that are comparable to the dye-dilution method, both on healthy individuals and patients with altered hemodynamics. The differences between the compared results are in the range of error of the method (6%). The reason for more significant differences in the early postoperative period should be sought in the specifics of alteration of hemodynamics and, in this regard, differences in recovery of vascular tonus.

The rheographic method has gained wide popularity in clinical practice to evaluate peripheral circulation. However, as a result of this investigation, it has been established that the method is capable of reflecting not only marked pathology, but circulatory changes related to functional disturbances in the vascular system. It was shown that the volumetric pulsed delivery of blood to the limbs is determined by local circulatory factors (extensibility, tonus of arteries, anatomic condition of the vessel), in addition to level of stroke volume of the heart. The use of rheography, and particularly tetrapolar rheography, for quantitative estimation of the main indices of central hemodynamics and peripheral vessels opens up a new avenue for examination of the functional state of one of the principal elements in the human circulatory system.

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BRIEF REPORTS

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CARBOHYDRATE AND LIPID CONTENT OF RAT LIVER TISSUE FOLLOWING A 22-DAY SPACE FLIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 75-76

[Article by R. A. Belitskaya, submitted 1 Sep 75]

[Text] Carbohydrate and lipid levels in liver cells are among the important indices of functional activity of the liver and homeostatic properties of producing glucose and lipids secreted into blood. Our objective here was to test the levels of total carbohydrates, lipids and phospholipids in hepatic tissue of rats that had been in a space flight.

We examined the rat liver 1 and 26 days after a 22-day space flight on the Kosmos-605 biosatellite, and 1 and 26 days after a ground-based experiment, in which the animals were kept in a spacecraft model, with simulation of all flight conditions, with the exception of weightlessness. The liver was taken after collecting blood under pentothal anesthesia, separation of some muscles and the heart. We also examined the liver of rats in three control groups. In the 1st control group, the rats were kept in the vivarium and they were sacrificed in the same way as the experimental animals. The 2d group was kept in the vivarium and sacrificed by decapitation. The animals in the 1st and 2d control groups, like the experimental ones, were on a special flight diet. The 3d experimental group was kept in the vivarium on the usual diet, and it was sacrificed by decapitation.

We assayed total carbohydrates [1], lipids [4] and phospholipids [3] in liver tissue, frozen in liquid nitrogen, immediately after it was extracted. The Table lists the findings.

Carbohydrate level in liver tissue was in the low normal range 1 and 26 days after the space flight, as well as 1 day after the ground-based experiment. The same carbohydrate content was demonstrated in the liver of the 1st control group. The fact that carbohydrates were at the lower limit of normal in the liver of all these rats is probably attributable to resection of some skeletal muscles prior to taking hepatic tissues, which created the conditions for breakdown of glycogen to glucose and flushing of the latter with blood from the liver. The higher carbohydrate content of the liver of

rats in the 2d control group could be attributed to the fact that hepatic tissue was extracted and froxen immediately after decapitation. Muscles were not resected in 2 rats examined 1 day after the flight, and the liver was rapidly frozen. The carbohydrate content of the liver of these rats constituted 4.0 and 4.40 g%. The same carbohydrate level was demonstrated in the liver of rats in the 2d and 3d control groups.

Carbohydrate, lipid and phospholipid levels in rat liver tissue

	Statist. indices	After flight		After ground-based exp		Control groups		
		1	26	1	26	1	2	3
Carbohydrates (g%)	M	2,35	2,80	2,30		2,20	4,20	4,40
	$\pm m$	0,54	0,58	0,52		0,11	0,30	0,48
	n	7	5	7		5	7	6
Lipids (g%)	M	8,50	6,40	7,90	5,70	6,50	5,70	4,60
	$\pm m$	0,92	0,51	0,46	0,48	0,30	0,22	0,18
	n	6	5	7	6	6	7	6
	P_1	<0,1		<0,05				
	P_2	<0,02						
	P_3					<0,01		
Phospholipids (µg phosphorus/g wet tissue)	M	1520	1160	1280	1060	1150	1010	1050
	$\pm m$	95	17	58	57	51	62	43
	n	7	5	7	6	5	7	12
	P_1	<0,01		<0,2				

Note: P_1, P_2 and P_3--as compared to the 1st, 2d and 3d control groups, respectively.

A comparison of experimental and control data shows that the carbohydrate level of the liver was in the normal range in rats involved in the 22-day space flight. Consequently, under space flight conditions, hepatic cells retain the capacity to maintain the required carbohydrate level for normal supply of glucose to tissues of the organism.

The lipid content of the liver showed a tendency toward increasing 1 day after the space flight, as compared to the 1st and 2d control groups. The lipid level of the liver returned to the one inherent in animals receiving the special inflight diet on the 26th day of the recovery period after the flight. It must be noted that the lipid level in the liver of rats kept on the special diet was higher than in animals given the usual diet. Assay of lipid content of the rat liver 1 and 26 days after the ground-based experiment revealed the same patterns as in the flight experiment: elevation of lipid level immediately after the flight and lowering to the control level after 26 days. This indicates that it is not weightlessness, but maintenance conditions, i.e., restricted mobility, gas environment, diet, etc., that play the leading role in raising the liver lipid level. Accumulation of lipids in hepatic tissue could be due to decreased lipid metabolism,

which is confirmed by the depression of lipid metabolism in rats, whose mobility was restricted for 90-150 days [5].

Phospholipid content of the liver was increased 1 day after landing, and it reverted to base levels after 26 days. We observed only a mild tendency toward elevation of phospholipid level of the liver 1 day after the ground-based experiment. Consequently, weightlessness intensified the changes in phospholipid metabolism of the liver, which occurred under the influence of restricted mobility. It is known that a physical load (swimming) leads to a decrease in total phospholipids of the liver [2]. For this reason, it may be assumed that expressly the decrease in muscular activity, under space flight conditions, leads to elevation of phospholipid level in the liver.

Thus, the 22-day space flight did not affect total carbohydrate content of the liver, but it did lead to an increase in lipids and phospholipids, which reverted to normal in the postflight period. However, the weightlessness factor could have elicited only an increase in phospholipids.

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CHANGES IN CIRCULATING BLOOD VOLUME AND FILLING OF THE BRAIN AND INTERNAL ORGANS OF RATS FOLLOWING ACUTE AND CHRONIC HYPOXIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 76-80

[Article by M. A. Kolesov and M. N. Shcherbakova, submitted 3 Feb 75]

[Text] Hypoxia elicits a number of adaptational reactions in the organism directed toward improved delivery of oxygen to tissues. Changes in blood indices play a substantial role in this respect. In the case of acute hypoxia, these changes are manifested by an increase in circulating blood volume (CBV) and in chronic hypoxia, by an increase in number of erythrocytes and hemoglobin content [4-6 and others].

Another important factor involved in assuring adequate delivery of oxygen in the presence of hypoxemia at the lung--tissue stage refers to morphofunctional changes in the circulatory system. It has been shown that while there is redistribution of blood, as a result of which blood supply to vital organs increases [7, 8, 14, 19] in the presence of acute hypoxia, blood supply to all organs is increased in the case of chronic hypoxia [9, 13 and others].

Analysis of the literature revealed that most studies were conducted during exposure to the hypoxic factor or immediately after. There are few works dealing with delivery of blood to different organs at the later stages [2, 21]. Moreover, the information about the reaction of the vascular system of some organs (for example, the lung and kidney) to hypoxia is quite contradictory.

Our objective was to investigate some blood indices, as well as filling of the brain and internal organs at various intervals after hypoxia in rats that were or were not adapted to hypoxia.

Methods

Experiments were conducted on 160 albino rats weighing 150-250 g. Acute hypoxia was induced by single elevation of rats in a pressure chamber to an "altitude" of 9000 m, where they remained for 1 hour. Chronic hypoxia was induced by daily ascents in the pressure chamber for 3-4 months.

The initial "altitude" constituted 4000 m and it was increased weekly by 500-700 m reaching 9000 m toward the end of the adaptation period. We gradually increased the time during which the rats were kept in the pressure chamber from 1 to 4 h. CBV was determined by the Evans' blue dye dilution test [23]. The rats were sacrificed by means of rapid immersion in liquid nitrogen to examine filling of organs. We prepared homogenates of the brain, heart, lung, liver, kidney, spleen and femoral rectus muscle in 0.007 M ammonia solution. The homogenates were centrifuged at 18,000 r/min for 20 min and blood per gram tissue was determined spectrophotometrically, according to amount of oxyhemoglobin.

Results and Discussion

Acute hypoxia: A 29% increase in CBV was demonstrated in rats that were kept at an "altitude" of 9000 m for 1 h and examined 5-10 min later (Table 1). Estimation of hematocrit index revealed that the change in CBV was due to an increase in number of erythrocytes. There was virtually no change in plasma volume. The blood indices did not differ substantially from normal after 1.5-2 h.

A study of filling of organs under these experimental conditions revealed (Table 2) that there is appreciable increase in filling of the brain (by 22.2%), heart (28.6%) and liver (38%), with decrease in the kidney (by 39.6%), muscles and spleen (33.4%) and lung (20.8%).

These findings are consistent with the results of other authors, indicating that, in the presence of acute hypoxia, as a result of the coordinated effect of neurohumoral and tissular factors, there is selective redistribution of blood in the direction of predominant filling of vital organs, in particular the brain and heart [8, 15, 19]. Evidently, this is due to the fact that the decreased oxidative phosphorylation, occurring with hypoxemia, leads to prevalence of ATP breakdown over resynthesis and, as a result, accumulation in tissues of products of ATP breakdown, which are an important factor in adaptational redistribution of blood flow [15, 18].

The pressure elevation in pulmonary vessels, which occurs with decrease in oxygen content of alveolar air, is related not only to an increase in minute volume, but mainly constriction of pulmonary vessels, and this is also confirmed by our data. The contradiction between our results and the data of M. M. Seredenko [16] is apparently due to the use of different methods of creating hypoxic conditions and sacrificing the animals. As we know, there is a correlation between the reaction of pulmonary vessels to a change in gas composition of inspired air and severity of hypoxemia [22]; moreover, this is a phasic reaction [20].

Determination of filling of organs 1 h after being in the pressure chamber revealed that it had not yet reverted to normal in virtually all organs. We were impressed by the decrease to 83.3% in filling of the brain, and this is evidently the result of hyperventilation which, as we know, leads to an increase in cerebrovascular resistance and decrease in cerebral blood flow.

Table 1. Results of determination of CBV, plasma volume and blood hematocrit index in rats

Blood indices	Control	Acute hypoxia (9000 m)		Chronic hypoxia (adaptation at 9000 m)			
		after 5-10min	after 1.5-2h	after 24 h	aft.10 days	aft. 20 d.	aft. 50 d.
CBV	5,72±0,28	7,38±0,42 $P>0,05$	5,33±0,33 $P>0,05$	8,70±0,56 $P<0,001$	6,66±0,41 $P>0,05$	6,47±0,32 $P>0,05$	5,87±0,22 $P>0,05$
Plasma volume	3,17±0,17	3,26±0,10 $P>0,05$	2,70±0,22 $P>0,05$	2,78±0,13 $P>0,05$	2,78±0,13 $P>0,05$	2,86±0,10 $P>0,05$	2,89±0,13 $P>0,05$
Hematocrit index	0,410±0,007	0,533±0,027 $P<0,001$	0,462±0,012 $P>0,01$	0,649±0,032 $P>0,001$	0,523±0,031 $P<0,01$	0,459±0,019 $P>0,05$	0,458±0,008 $P<0,001$

Table 2. Blood filling (ml/g tissue) in the presence of organic hypoxia

Organ	Control	Acute hypoxia		Chronic hypoxia				
		aft.5-10 min	aft. 1 h	aft. 24 h	aft.10days	aft. 20 d.	after 40 d.	after 60 d.
Brain	0,018±0,001	0,022±0,001 $P<0,01$	0,015±0,001 $P<0,05$	0,039±0,002 $P<0,001$	0,028±0,001 $P<0,001$	0,021±0,001 $P<0,05$	0,018±0,001	0,019±0,001 $P<0,5$
Heart	0,015±0,009	0,193±0,005 $P<0,001$	0,169±0,006 $P<0,1$	0,222±0,011 $P<0,001$	—	0,176±0,005 $P<0,01$	—	—
Lung	0,457±0,016	0,362±0,015 $P<0,001$	0,436±0,039 $P>0,5$	0,529±0,018 $P<0,01$	0,478±0,016 $P<0,5$	0,460±0,015 $P>0,5$	0,465±0,030 $P>0,5$	0,447±0,023 $P>0,5$
Liver	0,100±0,006	0,138±0,007 $P<0,001$	0,126±0,019 $P<0,2$	0,230±0,013 $P<0,001$	0,210±0,009 $P<0,001$	0,133±0,010 $P<0,01$	0,129±0,007 $P<0,01$	0,141±0,006 $P<0,001$
Spleen	0,180±0,012	0,119±0,024 $P<0,05$	0,149±0,032 $P<0,5$	0,263±0,030 $P<0,02$	—	0,223±0,031 $P<0,5$	—	—
Kidney	0,091±0,007	0,055±0,005 $P<0,001$	0,046±0,005 $P<0,001$	0,143±0,016 $P<0,01$	0,138±0,011 $P<0,01$	0,119±0,024 $P<0,5$	0,058±0,008 $P<0,01$	0,063±0,006 $P<0,01$
Muscle	0,015±0,001	0,010±0,001 $P<0,001$	0,012±0,001 $P<0,05$	0,019±0,001 $P<0,01$	0,018±0,001 $P<0,05$	0,014±0,001 $P<0,5$	0,014±0,001 $P<0,5$	0,015±0,001 —

We also demonstrated a decrease in amount of blood in the kidney, to 50% of the base level. A decrease in renal blood flow was also observed by other authors in the presence of hypoxic hypoxia [1, 11]. We do not concur with some authors, who believe that the kidney is an organ with a perfect system of regulation and that renal blood flow remains constant, even with significant changes in arterial pressure and flow in other organs and tissues.

Chronic hypoxia: The changes in blood indices of rats adapted to hypoxia (see Table 1) were more significant than in unadapted rats. Thus, 24 h after the last "climb," their CBV was 52.2% higher than in control rats, hematocrit indices was 58.2% higher, while plasma volume was 12.4% lower. By the 10th day of adaptation to hypoxia, CBV and the hematocrit index dropped significantly, and constituted 16.4 and 27.5% more, respectively, than in the control. Plasma volume was 7.3% less than in the control. Thereafter, CBV gradually decreased and by the 50th day it was the same as in control rats. At the same time, the hematocrit index remained 11.7% higher than in the control, apparently as a result of diminished plasma volume (91.1% of the base level). As we see, the increase in CBV under the influence of chronic hypoxia occurs primarily due to intensification of erythropoiesis. This is based on activation of nucleic acid and protein synthesis in the system of red cell reproduction under the influence of hemopoietins and products of hemoglobin breakdown [3, 15, 17].

Determination of filling of organs with blood in hypoxia-adapted rats (see Table 2) revealed an increase in amount of blood in all organs, but not to the same extent. There was the most marked increase in filling of the brain (by 116.6%), liver (130%), heart (48%), kidney (57.1%) and spleen (46.1%). There was a less marked increase in filling of muscle (26.6%) and the lung (15.7%). With increase in time after the end of adaptation, there was gradual decrease in filling of organs. The most appreciable decrease in amount of blood was observed in the brain and lungs for the first 10 days, whereas in the liver, muscles and kidney this was seen only on the 20th day or later. Analogous results, with regard to filling of the brain, were obtained by one of the present authors [10] in a morphological study of blood vessels. In most organs, the amount of blood was close to base levels on the 40th and 60th days.

On the basis of the literature and our results, it can be concluded that acute hypoxia induces redistribution of blood flow in the direction of predominant delivery of blood to the heart, brain and liver, at the expense of decreased delivery to all other organs. These changes are transient and functional in nature. Under the influence of chronic hypoxia (intermittent adaptation to hypoxia), there is intensified delivery of blood to all examined organs, and this is indicative of the substantial role played by the transport factor in adaptation to hypoxia. As a result of multiple exposure of animals to a hypoxic environment, the changes in the vascular bed become structurally fixed and they are demonstrable for a long time. There is some correlation between the change in CBV and filling of organs in the presence of acute and chronic hypoxia.

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THE HEMATIC SYSTEM IN THE SET OF SYMPTOMS OF AUTONOMIC DISORDERS IN MONKEYS ON THE 'LOW GRAVITATION' STAND

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 80-83

[Article by G. S. Belkaniya and M. I. Kuksova, submitted 13 May 75]

[Text] The interest in hematological characteristics of the effects on monkeys of lowered gravitation is due to the rather distinct changes that occur in peripheral blood of cosmonauts during space flights. It is also a pressing matter to study the hemopoietic system as related to demonstration of additional evidence of similarity of the model of "lowered gravitation" studied and weightless conditions. In addition, it is possible to make a more comprehensive clinical and experimental analysis of reduction of erythrocyte mass, erythrocyte resistance, hemoglobin content, thrombocytes in blood, neutrophilic leukocytosis and lymphopenia, which are observed during space flights [9, 6].

In a previous work [1], we described the general physiological effects of a "low gravitation" stand, which was based on the principle of tilted suspension of animals. The present work deals with analysis of the reaction of the hematic system as a component of the vegetative set of symptoms, which enables us to make an integral evaluation of the physical condition of animals and demonstrate the effects of the simulated low gravitation conditions. Furthermore, we considered the possibility of determining the extent to which the antigravity reaction is mediated through the hemopoietic system.

Experiments were conducted on 8 Macaca rhesus monkeys ranging in age from 3 to 5 years. We used the conventional methods [5] to examine the morphological composition of peripheral blood and bone marrow. The hematological indices were compared to the state of autonomic and somatic functions. We conducted 6 experiments, in which the monkeys were exposed to a "low" gravitation load for 3, 7, 14 and 20 days, two experiments with 26-day exposure and 4 control experiments. In the control experiments, all of the conditions, with the exception of tilted suspension, of the main experiment were retained; the monkeys moved about with the body in the usual position

and with ordinary gravitation in the static vector. Figure 1 is a diagrammatic illustration of experimental conditions.

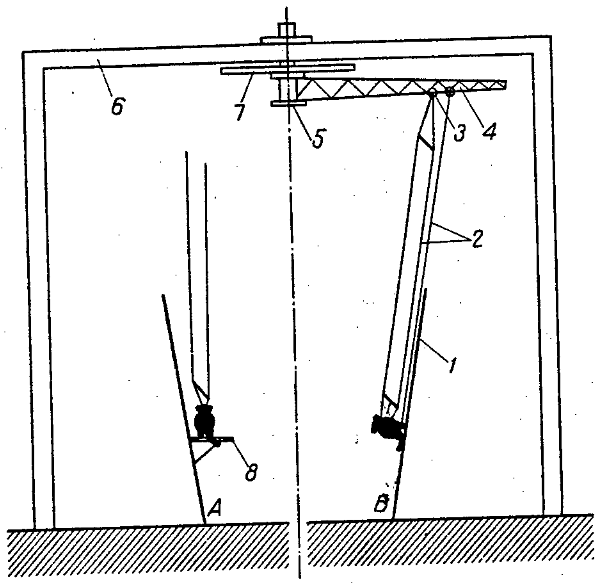

Figure 1.
Diagram of stand conditions

A) control experiment, usual gravitation static [bearing] load
B) main experiment, low gravitation load in static vector
1) wall of cone tilted at an angle of 9°36' from gravitation normal
2) suspension system
3) attachment unit of suspension system
4) sliding truss revolving around moving axis (5)
6) support construction
7) current collector for derivation of physiological information
8) circular horizontal platform for control experiment

For the first few hours of exposure to low gravity, we observed psycho-emotional tension while adjusting to the experimental situation. There was motor excitation, with faster pulse and respiration, elevation of systolic and diastolic pressure. Red blood indices did not change appreciably, while the changes in composition of white blood were more distinct: increase in total leukocyte content, absolute and relative neutrophilia, lymphopenia and eosinopenia. The reaction was analagous for the first few hours in the control experiment.

In most monkeys, there were two phases to the leukocytic reaction during the period on the stand (Figure 2). The first phase lasted 4 to 10 days and was characterized by leukopenia with a neutrophil shift, absolute and relative lymphopenia. In this same phase, there was a decrease in hemoglobin, erythrocytes and reticulocytes, with persisting eosinopenia, and the hematocrit index dropped. Such dynamics of changes in composition of peripheral blood could, to some extent, be indicative of functional depression of hemopoiesis. This conclusion is quite valid, if we consider that it is expressly during this period of being on the stand that the physiological systems change, after the primary reaction, to a lower functional level.

With continued presence on the stand, after the relative leukopenia of the first phase, there was moderate neutrophil leukocytosis with a faster ESR [erythrocyte sedimentation rate] (second phase of leukocytic reaction). In peripheral blood, a small amount of eosinophils appeared; the absolute number of lymphocytes increased, in spite of the fact that the relative index remained below the base level. In this phase, the absolute amount

of white blood cells increased, as compared to both the first phase of the leukocyte reaction and the initial levels. In this case, it may be assumed that the hematic system changes its functional level which, making certain assumptions, could be related to processes of adaptation to the stand conditions. The assumption is related to the fact that hematological changes reflect the actual reaction of the hematic system to developing internal homeostatic stress in the organism of monkeys.

In the second phase of the leukocytic reaction, we observed apparent activation of erythropoiesis, in addition to neutrophil leukocytosis. There was some increase in peripheral blood erythrocytes and reticulocytes, although there was a concurrent elevation of hematocrit index. Most probably, these changes are related to a decrease in plasma volume, rather than true activation of erythropoiesis. Intensification of diuretic activity (Henry-Gauer reflex) plays some part in the origin of these changes. In all experiments lasting at least 14 days, we observed a decrease in overall number of erythroblast elements in bone marrow. While the relative amount of erythroid cells was in the range of 22-53% in the prestand analysis, it constituted 13-24% after the stand, with a mean 49% decrease in erythroblast elements of bone marrow in all of the experiments. With inhibition of erythropoiesis in the bone marrow, there was asynchrony between synthesis of hemoglobin and loss of nucleus of erythroblast elements [2, 10, 11], and this was associated with appearance of or increase in amount of poikilocytes, anisocytes and polychromatophil erythrocytes in peripheral blood. In addition there was increased hypochromia of erythrocytes. In the 26-day experiments, there was a decrease in osmotic resistance of erythrocytes. Analysis of the literature [8, 7] shows that a certain intensity of erythropoiesis is assured by the normal tonus on all levels of the nervous system, which mediates its influence on erythropoiesis through neurohumoral mechanisms. Apparently, the static reaction and level of general motor activity are very important to formation of normal tonus of the functional regulatory complex, and through it of erythropoiesis. In the stand, both these factors are defective: the static load as the primary one and a mandatory condition of the experiment, and general motor activity as the secondary one, resulting from the change in functional state of the organism. Thus, there are very real prerequisites for hypofunction of the erythropoietic system. It is opportune to refer here to the well-known works [3, 4], in which there is rather argumented demonstration of the correlation between functional activity of medullary hemopoiesis and relative gravistatic tension and level of the animal's motor activity.

The lack of changes in erythroblast activity in three control animals and increase in erythroblast elements in the bone marrow of one animal serve as additional evidence of the fact that the observed depression of erythropoiesis occurs as a result of a diminished static load. It should be borne in mind that, in control animals with the usual level of the static reaction, in spite of the continued presence of a set of situational and psychoemotional stimuli, we failed to observe changes inherent in conditions of low static load [1]. In control experiments, the animals gained weight; their physical condition was good and they presented no vegetative or statokinetic disorders.

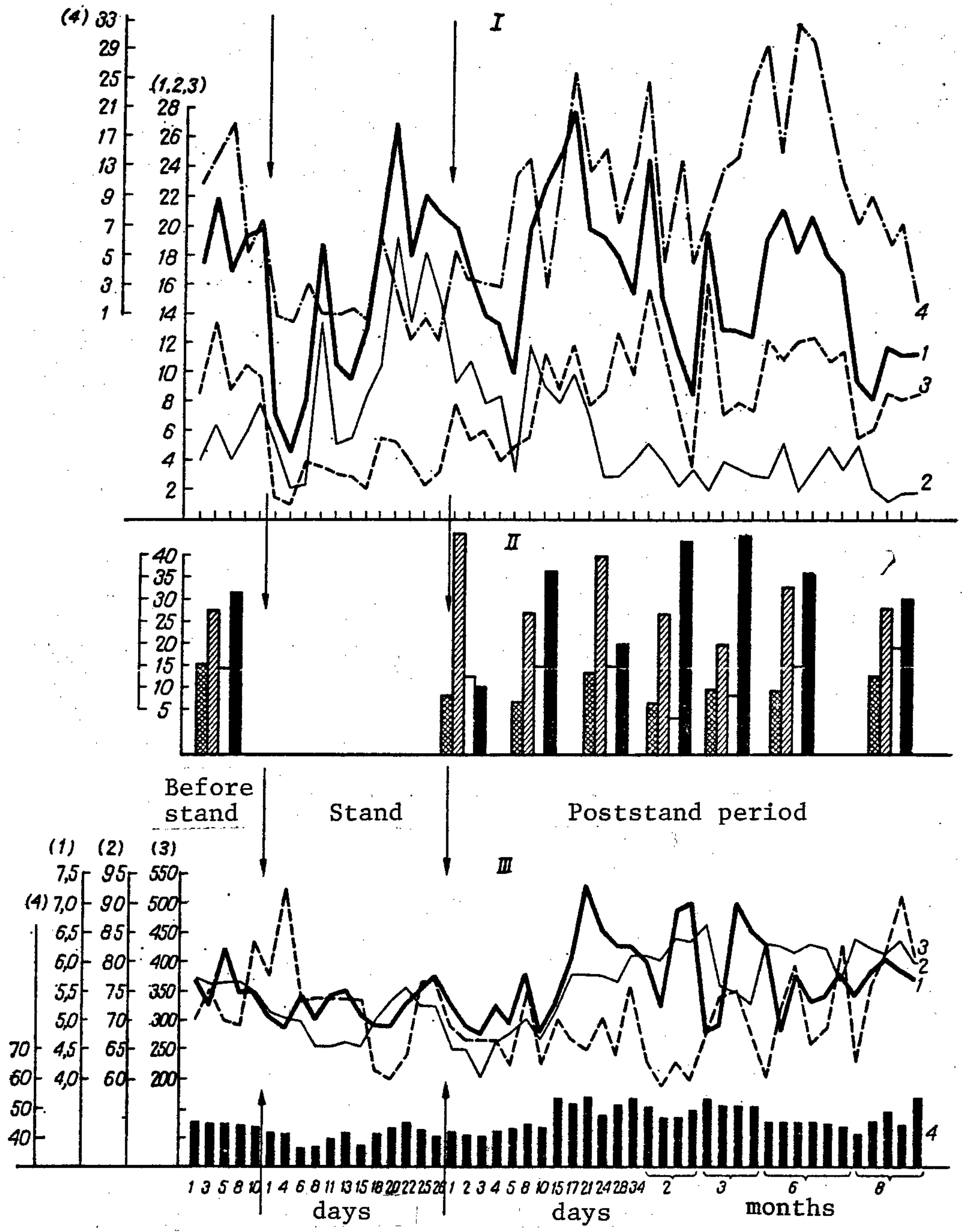

Figure 2. Dynamics of hematological indices of monkey No 10508 during 26 days on "low gravitation" stand and readaptation period

I: 1) leukocytes (thousands)
2) neutrophils (thousands)
3) lymphocytes (thousands)
4) eosinophils (hundreds)

II) bone marrow indices (%):
1st column--young white cells
2d column--mature neutrophils
3d column--lymphocytes
4th column--erythroid cells

III: 1) erythrocytes (millions)
2) hemoglobin (%)
3) thrombocytes (thousands)
4) hematocrit index (%)

During the control period on the stand, there was a rather high level of general motor activity in the monkeys, and it increased as the animals adjusted to the experimental situation. Since the main experimental factor was eliminated from the control experiments, i.e., the lowered gravitation load in the static vector, it may be assumed that the chief cause of the entire set of disorders on the "low gravitation" stand and, in particular, decreased erythroblast activity of bone marrow, is the decreased static reaction, which is one of the main regulatory components of interaction between the organism and ambient gravitation and formation of the functional system providing for antigravitation function of the organism.

In the aftereffect period, we observed signs of stimulation of hemopoiesis, as reflected by increasing erythroblast activity of medullary hemopoiesis: there was an increase in erythroid cells on the myelogram, and an increase in amount of erythrocytes, reticulocytes and hemoglobin in blood. Erythroblastosis was particularly marked after restoration of the usual characteristics of the static reaction and motor activity of the monkeys. In addition, the poststand period was characterized by marked lability with regard to composition of peripheral blood, and this corresponded to instability of autonomic regulation of other physiological systems of the organism and persistence of marked orthostatic insufficiency. In this regard, we must stress the rather high informative value of hematological indices of monkeys, which permit rather distinct observation of dynamics of autonomic changes, both while the animals are in the stand and in the readaptation period.

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RELATIONSHIP BETWEEN ONSET OF ALTITUDE-DECOMPRESSION DISORDERS IN MAN AND BAROMETRIC PRESSURE LEVEL DURING INTENSIVE PHYSICAL EXERCISE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 4, 1977 pp 83-85

[Article by M. I. Vakar, A. N. Mazin, A. S. Tsivilashvili and V. V. Mal'chikov, submitted 3 Jun 75]

[Text] The information in the literature concerning the incidence of altitude-decompression disorders (ADD) at high altitudes is quite contradictory. For example, according to the data of Hitchcock [2], the incidence of ADD at 10,000 m is 7.6%. At the same time, in more recent works, American authors voice the opinion that the percentage of ADD, even at 8500-9000 m, is 40% with exposure of man to such altitudes for no more than 15 min. For a long time, an altitude of 7000 m was considered safe, from the standpoint of possible onset of ADD; however, according to the data of P. M. Gramenitskiy [1], the incidence of ADD constituted 54% (58 cases out of 107) in the case of 6-h exposure of subjects to 7000 m altitude and performance of physical work, and 63% (44 out of 70 cases) at 8100 m. Such information questions the desirability of creating a pressure of 0.4 atm in special gear.

We undertook the present study in view of the great importance of this question to aerospace practice.

Methods

Studies were conducted using a type SBK-48M pressure chamber, at "altitudes" of 7000 and 8150 m, which corresponded to excess pressure of 0.3 and 0.35 atm, respectively, in the pressure suits. All ascents were made without prebreathing, at maximum speed (in 1-1.5 min). During the "climb" and entire period at the altitude tested, the subjects breathed pure oxygen. Upon reaching the set altitude and after recording the main physiological indices, the subjects immediately began to perform physical work. In all, in the 6 h they spent at the given altitude, they performed 5-6 cycles of work. Each consisted of 40 min work and 20 min of rest. The nature of the work was to lift and lower a 15-kg weight to 70 cm at the rate of 30 times per min, stepping on a 35-cm step and down again at the same rate. They

performed these exercises alternately. In some experiments, a special physical load stand was used, to make it possible to exercise the upper and lower limbs simultaneously. In all instances, energy expenditure constituted 400-450 kcal/h.

We evaluated the subjects' general condition in accordance with the results of continuous medical monitoring of their general condition and recording of the main physiological parameters: heart and respiration rate, bioelectric potentials of the myocardium (EKG in three standard and two chest leads), temperature of the body and integument in five points (forehead, chest, back, arm, thigh). Some aspects of higher nervous activity, bioelectric activity of the cerebral cortex, Landolt tables and an electromechanical pencil were taken into consideration in the evaluation. Expenditure of energy was determined by the method of indirect calorimetry, using gas chromatographs.

The subjects' own reports also served as indices of their general condition during and after the experiment. We assessed efficiency on the basis of adequacy of subjects' responses, correct and prompt performance of the experimenter's assignments and retention of coordination of movements. In the case of development of ADD, the subjects were hospitalized for 24 h, during which they were submitted to a comprehensive clinical examination. We conducted 483 tests involving 70 men, ranging in age from 20 to 40 years. A total of 434 tests were made at a pressure of 0.4 atm and 49, at 0.35 atm.

Results and Discussion

As a result of these studies, it was established that ADD developed in only 2 out of 434 cases (0.41%) when ambient atmospheric pressure was lowered from 1.0 to 0.4 atm (308 mm Hg) and in the absence of preliminary prebreathing. ADD developed in a mild, discrete form, and it disappeared rapidly with elevation of pressure. When ambient pressure was dropped to 0.35 atm, there was an appreciable increase in incidence of ADD: 8 out of 49 cases (16.3%). It was manifested in a more marked form and, in some cases, in the form of severe pain in the muscles and joints. As we have already mentioned, somewhat different data were obtained by P. M. Gramenitskiy. The discrepancy of results could be attributed to different experimental conditions and, primarily difference in intensity and nature of physical exercises. In the studies of P. M. Gramenitskiy, the subjects exercised for 90 min, while the estimated expenditure of energy constituted about 250 kcal/h. In our studies, the exercises lasted longer. This warrants the assumption that the probability of ADD at this level of rarefication is related not only to the level of energy expended and duration of exercises, but nature of the latter. The question of correlation between incidence of ADD and nature and intensity of physical exercise performed by a man requires further investigation.

With onset of ADD we observed an increase in time required to write down letters, words and in intervals between them, with decrease in capacity of the visual analyzer. All this was indicative of intensification of the

inhibitory process in the cerebral cortex. Concurrently, we observed elevation of rectal (0.5°) and weighted mean (by 1-1.5°) body temperature, which should apparently be interpreted as a distinctive nervous reflex reaction accompanying decompression disorders.

According to the medical observations, at the time of onset of ADD the subjects presented some sluggishness, listlessness and apathy. There was impairment of coordinated movements in performing some tasks and following some directions of the experimenter, as well as a change in handwriting. We failed to demonstrate patterns to the change in autonomic functions of the subjects with onset of ADD. In some cases, with onset of ADD, there was a 20-24/min increase in heart rate, 3-5/min increase in respiration and decrease (by 20-30 s) in breath-holding time in inspiration. However, in most cases, there were no changes referable to the cardiovascular and respiratory systems. The observed changes were typical for individuals performing heavy physical labor.

It must be noted that the 2 cases of ADD occurring at an altitude of 7000 m were manifested in a mild form, and clinical examination failed to demonstrate deviations from normal with regard to functional systems of the body. At the same time, with onset of ADD at 8150 m, most subjects presented accentuation of tendon and plantar reflexes with positive response, development of generalized and distal hyperhidrosis, tremor of the eyelids and extended fingers. In some cases, accentuation of tendon and periostal reflexes was associated with rapid depletion of abdominal and plantar reflexes, as well as signs of oral automatism (palm-chin and lip reflexes). General medical examination failed to demonstrate pathology. However, according to rheoencephalographic and rheovasographic data, virtually all of the subjects presented moderate asymmetry of amplitudes, without significant change in tonus and other properties of vessels. Subject K-n presented significant asymmetry of amplitudes in the upper limbs and Kr-v presented a hypertensive type of rheograms. These changes could be evaluated as signs of involvement of the brain stem, with predominant reference to vasomotor and motor centers.

Thus, the experimental data obtained enable us to conclude, with enough certainty, that there is a borderline between 0.4 and 0.35 atm, exceeding which causes a sharp increase not only in incidence of ADD, but in severity of clinical manifestations thereof. The presence of appreciable signs of impaired function of the central nervous system, including the autonomic centers, warrants the belief that the change from 1 atm to 0.35 atm is hazardous and could lead to severe impairment of man's general physical condition.

This conclusion also applies, in the case of changing to a lowered pressure of 0.35 atm without prebreathing. The effectiveness of the latter has not yet been established, and it requires further experimental investigation.

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PREVENTION OF HYPERTENSIVE STATES IN SHIP CREWS OUT AT SEA

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No 4, 1977 pp 85-87

[Article by V. N. Barnatskiy, A. G. Kuznetsov, V. A. Kotenko, B. I. Goryayev, M. V. Pimenova and Yu. S. Slobodchuk, submitted 31 Jan 75]

[Text] Pathology of the cardiovascular system, and particularly essential hypertension, is one of the causes of diminished fitness of seamen and subsequent grounding for health reasons. For this reason, prevention and treatment of this disease constitutes one of the important tasks for medicine. At the present time, effective hypotensive agents, referable to the group of potent drugs, are used extensively in the treatment and prevention of essential hypertension. In addition, a method of normalizing the activity of the cardiovascular system, based on the use of chemicals which, under natural conditions, are directly involved in metabolic processes and do not elicit excessive stress on systems responsible for maintaining the most important constants of the body's internal environment, merits attention. Studies conducted on ships in the course of long-term cruises established that no arterial pressure drop was observed during storms among seamen susceptible to seasickness after intravenous and rectal administration of sodium hydrocarbonate ($NaHCO_3$), whereas it did drop significantly in a control group. Concurrently, it was observed that $NaHCO_3$ had a hypotensive effect on seamen with high arterial pressure. Studies were conducted at different latitudes in the ocean to test the hypotensive effect of NaHCO on ship crews. It was planned to develop methods of using $NaHCO_3$ to prevent hypertensive states in seamen.

Methods

Studies were conducted on freezer fishing trawlers (FFT), large freezer trawlers (LFFT), floating bases and reffrigerator ships in the tropical and temperate latitudes of the Atlantic Ocean. $NaHCO_3$ was given intravenously only on the floating bases, where it was used at the rate of 0.075 g per kg body weight. $NaHCO_3$ was injected using a blood transfusion system. In the presence of diastolic pressure (DP) of 85-95 mm Hg, 6 intravenous injections were ordered in a dosage of 150-180 ml each of 4% $NaHCO_3$ at 3-day intervals; with DP of 95-105 mm Hg, 8-10 injections in the same doses

were given at the same intervals. Rectal administration of $NaHCO_3$ in suppository form was prescribed with DP of 85-95 mm Hg, once or twice a day for 3 weeks, each suppository containing 0.7, 0.5 or 0.03 g $NaHCO_3$. The course was repeated after 1 week. With DP of 95-105 mm Hg, administration of $NaHCO_3$ was performed following the same programs to the end of the cruise. We began to give $NaHCO_3$ after 2-3 weeks of control measurements of arterial pressure by the method of Korotkov, and mandatorily repeated after 1 week on the cruise. In the control group, arterial pressure was measured throughout the cruise. We used the Starr formula to determine minute volume of blood (MV) and the Poiseuille formula for total peripheral resistance of vessels. As an additional control, we took a group of seamen with normal pressure. Some of this group was given $NaHCO_3$ as described above, and the rest of the group was a control.

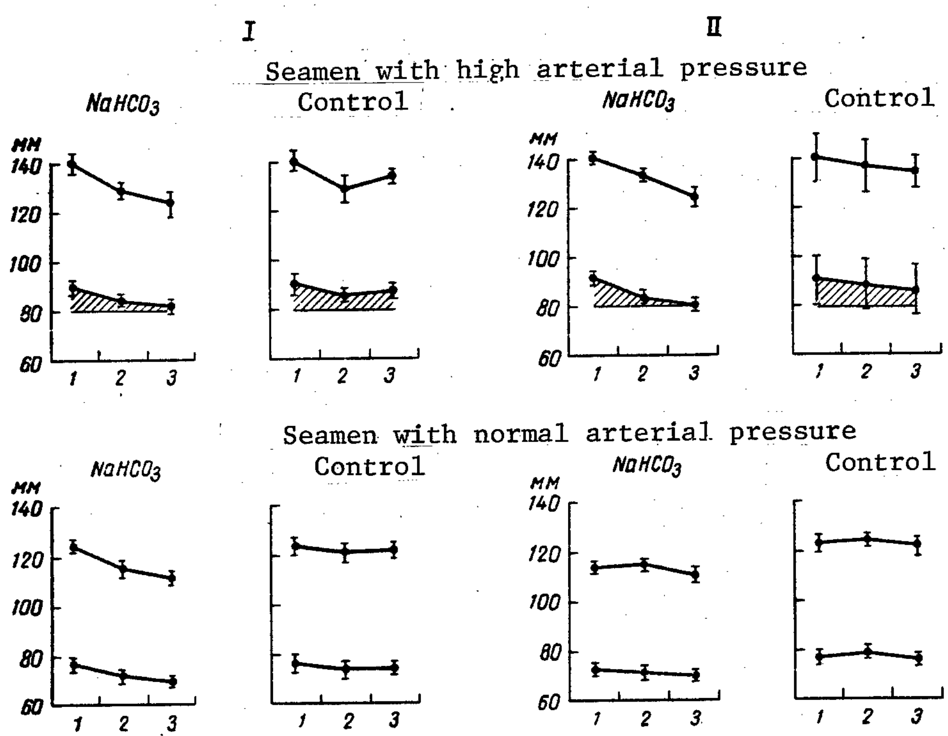

Figure 1. Systolic and diastolic pressure of seamen with high and normal arterial pressure in the tropics (I) and temperate latitudes (II), before and after administration of $NaHCO_3$

Top curve, systolic and bottom, diastolic pressure. Severity of hypertension (excess of diastolic pressure from the 80 mm Hg line) is marked in black. X-axis, cruise duration; y-axis, arterial pressure, mm Hg. The confidence intervals are given for $P = 0.05$.

Here and in Figure 2:
1) start of cruise 2) middle 3) end of cruise

Results and Discussion

In all, 237 men had been examined as of 1 Dec 73, 160 of whom were given $NaHCO_3$ intravenously or rectally, while 68 constituted the control group. Elevated arterial pressure was found in 126 people and it was normal in 111. Intravenous and rectal administration of $NaHCO_3$ elicited a distinct hypotensive effect in the seamen with high pressure, and it was observed for several weeks. In seamen whose DP was in the range of 85-95 mm Hg, it stabilized at normal levels after courses of intravenous or rectal $NaHCO_3$. In seamen who presented a DP of 95-105 mm Hg before $NaHCO_3$, it dropped by 10-15 mm after $NaHCO_3$ but did not reach normal levels. Concurrently, we observed improved general condition, diminished headaches during storms, as well as at high ambient air temperatures and humidity, among those who took $NaHCO_3$. Administration of $NaHCO_3$ to seamen with high arterial pressure in both the tropics and at temperate latitudes of the ocean caused a reliable drop of diastolic and systolic pressure, whereas in the control group the drop of diastolic pressure in the tropics and temperate latitudes was unreliable. As can be seen in Figure 1, the drop of systolic and diastolic pressure after administration of $NaHCO_3$ to seamen with normal arterial pressure was negligible but reliable in the tropics, while the decline of systolic pressure was unreliable at temperate latitudes.

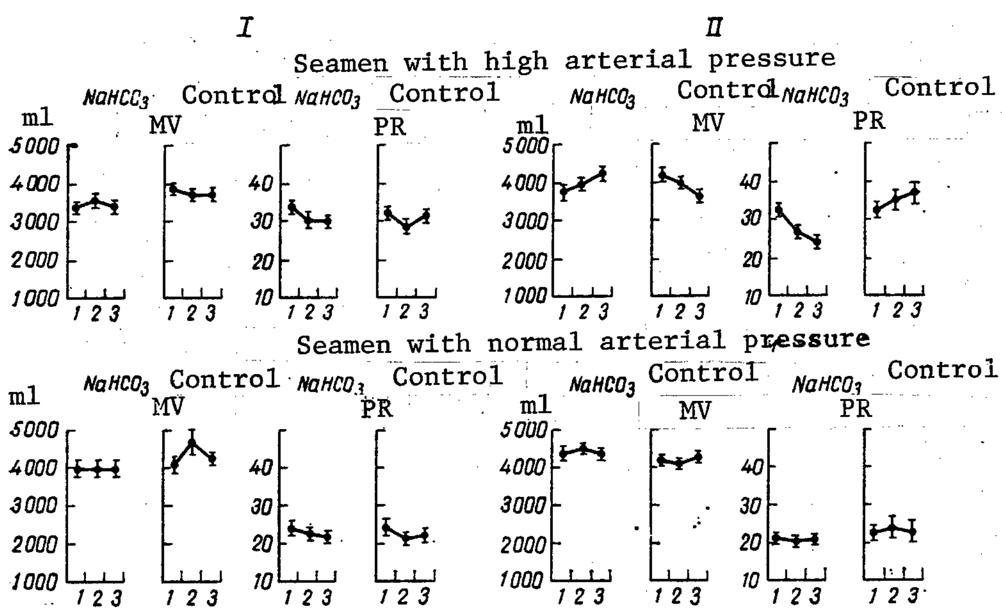

Figure 2. Changes in minute volume of blood (MV), total peripheral resistance of vessels (PR) in seamen with high and normal arterial pressure in the tropics (I) and temperate latitudes (II) before and after administration of $NaHCO_3$

X-axis, stages of the cruise; y-axis, MV in ml and PR in R units.

Administration of $NaHCO_3$ to seamen with normal arterial pressure, both in the tropics and temperate latitudes, failed to lower the pressure.

In the tropics, there was no change in MV after administration of $NaHCO_3$ to seamen with high arterial pressure, as well as crew members constituting the control group. Total peripheral resistance of vessels (PR) diminished reliably after administration of $NaHCO_3$ in seamen with high arterial pressure and did not change in the control group.

At temperate latitudes, there was a reliable increase in MV after administration of $NaHCO_3$ in seamen with high arterial pressure, but it did not exceed appropriate levels. In the control group, there was a reliable decrease in MV. PR diminished reliably in seamen with high arterial pressure after administration of $NaHCO_3$ and increased in the control group, but the latter was reliable with $P = 0.1$.

As can be seen in Figure 2, MV and PR levels in seamen with normal arterial pressure, both at temperate latitudes and in the tropics, were identical in the control after administration of $NaHCO_3$.

On 24 ships, we determined the amount of table salt (NaCl) supplied to the galley to prepare food, in order to investigate the causes of morbidity among crew members on a cruise. On 22 vessels, a mean of 25-30 g NaCl was consumed per person, and on the other 2 ships, 20 g NaCl per person, which is considerably higher than the physiological requirement. At the present time, the daily NaCl norm is 8-12 g. Consequently, on these vessels, intake of NaCl was above normal, even with consideration of their cruise in the tropics.

CURRENT EVENTS

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FOURTH ALL-UNION SYMPOSIUM ON RADIOTELEMETRY IN PHYSIOLOGY AND MEDICINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 4, 1977 pp 88-89

[Article by V. V. Rozenblat, R. M. Bayevskiy and A. D. Yegorov]

[Text] Biological radiotelemetry is acquiring increasing significance among the promising investigative methods that make wide use of the advances of modern electronics to solve biomedical problems. The 4th All-Union Symposium on Radiotelemetry and Physiology and Medicine dealt with the achievements in development thereof in the last 8 years and objectives of future work; it convened on 14-16 June 1976 in Sverdlovsk, the city where the 3 preceding symposiums also convened (1959, 1963, 1968). The symposium was conducted by the Scientific Council for Cybernetics of the USSR Academy of Sciences and RSFSR Ministry of Health.

There were three sections on the agenda of the symposium: general problems of bioradiotelemetry, engineering-methodological and biomedical. In all, 64 papers were submitted for discussion at the symposium. The proceedings of the symposium were published before it convened.

After the introductory remarks of V. V. ROZENBLAT, I. T. AKULINICHEV delivered a brief speech in memory of V. V. Parin who had chaired the previous meetings in Sverdlovsk.

R. M. BAYEVSKIY, I. I. BRYANOV and A. D. YEGOROV described the prospects of development of biotelemetry systems on orbital space stations. The authors based themselves on both theoretical analysis and generalization of data obtained during space flights and ground-based model experiments. The structure of a bioradiotelemetry system (BRTS) on a permanent orbital station could be described in the form of two subsystems: a) permanent equipment for operational medical monitoring with three modes of operation, continuous, periodic and emergency; b) periodically functioning equipment for in-depth medical monitoring and prognostication, also with three modes of operation, dynamic medical monitoring (about once a week), dispensary supervision (about once a month) and diagnostic tests when indicated or to obtain additional information. A list of 23 medicophysiological methods was compiled for use under the above conditions. V. V. Rozenblat discussed

the status and prospects of development of dynamic bioradiotelemetry, which permits observation of functions of a freely moving object. In the area of development of equipment and methods, the most important directions were the medical specifications for a dynamic radiotelemetry system, refinement of criteria for evaluation of BRTS (particularly methods of modulation in multichannel systems and increasing noise stability of BRTS). The author considers it an important task to broaden the range of monitored parameters, electrical activity of the heart, arterial pressure, respiratory functions, gas composition of expired air, etc. A large amount of data of a scientific instructive and applied nature has been accumulated as a result of telemetric studies of physiology of the active organism. In particular, by means of EEG telemetry, onset of fluctuations of bioelectric potentials has been demonstrated; the so-called stress [or tension] rhythms, as a result of intensive mental and neuroemotional tension (S. S. GOFMAN); the physiological norms of functional tension of the organism when performing heavy labor were substantiated on the basis of pulsometry data (YU. G. SOLONIN); the presence of "tension extrasystole" has been demonstrated in athletes (A. T. VOROB'YEV). V. M. KOLESNIKOV and V. M. AKHUTIN discussed promising directions of development of BRTS in applied human physiology. The paper of YA. V. FREYDIN submitted data on technology of modern bioradiotelemetry, particularly with reference to foreign efforts.

In the engineering-methodological section, V. V. ROZENBLAT and I. L. POPOV analyzed the informativeness of dynamic bioradiotelemetry on man. The authors proposed three restrictions to obtain the necessary and sufficient volume of information, as well as to rule out superfluousness, which deal with: a) the number of parameters examined (19 indices were chosen), b) capacity of communication channel (up to 1000 bits/s with maximum of 100 Hz frequency of useful signal) and c) volume of synchronously telemetered data (4 channels). The paper of YA. V. FREYDIN discussed the principles of multichannel biocardiotelemetry and substantiated the desirability of channel time sharing, using the method of dual amplitude and pulse modulation developed by the author. V. P. BAKALOV et al. (Novosibirsk) dealt with specific problems of noise stability. L. S. RUBIN reported on time-related recording of pulses with amplitude fading and the effect of fluctuating interference on pulse time fixing. YE. Z. TEMKIN discussed interchannel interference in magnetic recordings with pulsed modulation. V. P. BAKALOV and G. A. ABDULINA spoke about the control of physiological interference when using lateral feedback. The choice of signal frequency in biotelemetry was the subject of E. I. RIMSKIKH, A. I. TUROV and YU. A. KUKUSHKIN. P. P. KHORMA (Tartu) submitted data on methods of biotelemetry of a flying bird. A. I. TUROV and E. I. RIMSKIKH described a system of five-channel equipment with pulse modulation for picking up, transmitting, magnetic recording and input into a digital computer of physiological information.

L. S. RUBIN shed light on combining heterogeneous flows of information (physiological and hygienic data) in systems with variable cycle. R. A. YEFANOVA (Voronezh) spoke about comprehensive [complex] studies of the man--machine--environment system with recording of physiological data and characteristics of performed actions and parameters of the environment; she also shed light

on methods of studying work operations. YU. L. KAMINSKIY and M. YU. SIMONOV described a system of recording biotelemetry data in inputting them in an electronic digital computer. Several papers dealt with development of different elements of equipment, methods and devices for processing information.

The following delivered papers in the biomedical section: V. S. GENES, on methodological approaches to processing of bioradiotelemetry data; YU. V. LYSENKO, YU. P. OZEROV and B. V. PERMYAKOV, on a method of investigating transmission function of biosignals to improve effectiveness of analysis thereof; A. I. TUROV and B. A. MEN', on the use of the Monte Carlo method in cross-correlation analysis of EEG, with rejection of fixed equal intervals in quantation of segments of analyzed curves (the latter does not permit demonstration of high-frequency periodic components); V. L. GUREVICH and I. F. VAYSBURG, on preparation of bioradiotelemetry data for use in some pattern recognition algorithms. B. M. STOLBUN et al., and others submitted data on radiotelemetric characteristics of the EKG, velocity of pulse wave and sphygmograms during activity related to intensive mental and neuroemotional tension. Radioelectroencephalographic data were contained in the papers of G. K. BOGDANOVA. A group of studies dealt with the use of endoradioprobes: V. S. AVER'YANOVA et al. discussed confirmation of the diagnostic significance of data pertaining to pH of gastric contents with the use of radiocapsules, etc. Finally, S. KH. TATOYAN and G. S. BELKANIYA reported on radioelectrocardiography on monkeys and discussed some problems of ecological physiology of primates.

During the symposium, there was an exhibit of telemetry equipment. A number of multichannel systems with time and frequency sharing channels, as well as other instruments were displayed.

A decision adopted by the symposium listed recommendations that would implement continued development of bioradiotelemetry in the USSR. It is planned to hold the next symposium in 1980-1981.

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